#4

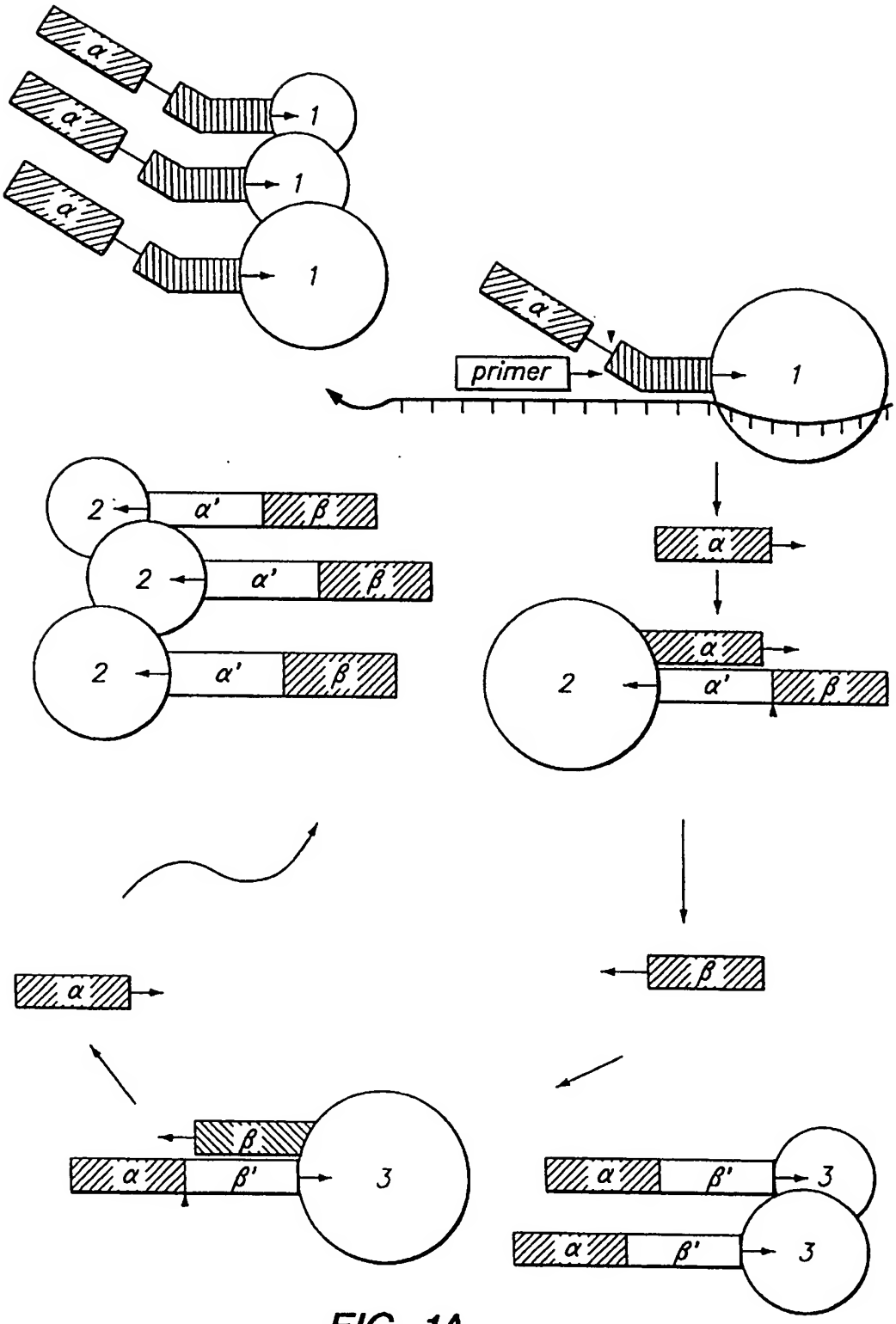


FIG. 1A

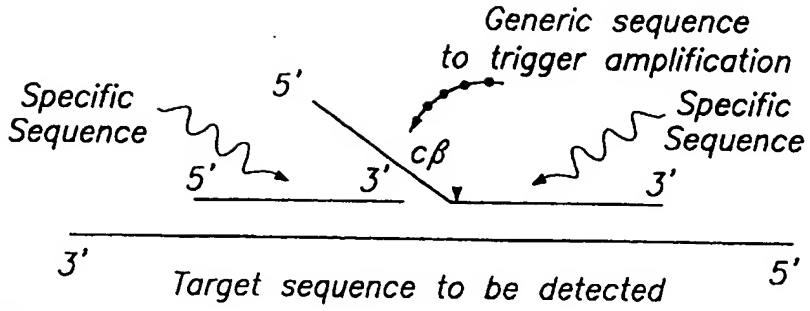


FIG. 1B PART ONE: TRIGGER REACTION

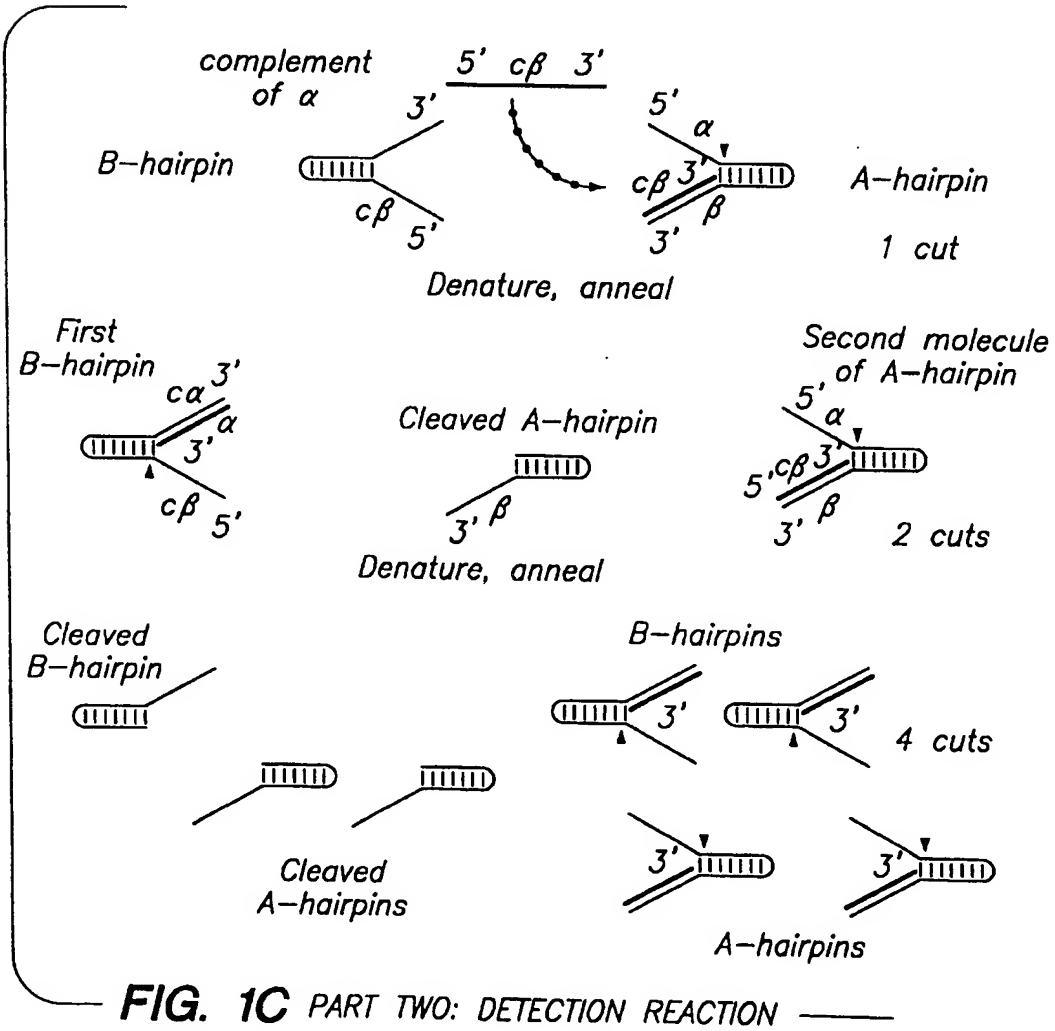


FIG. 1C PART TWO: DETECTION REACTION

FIG. 2A

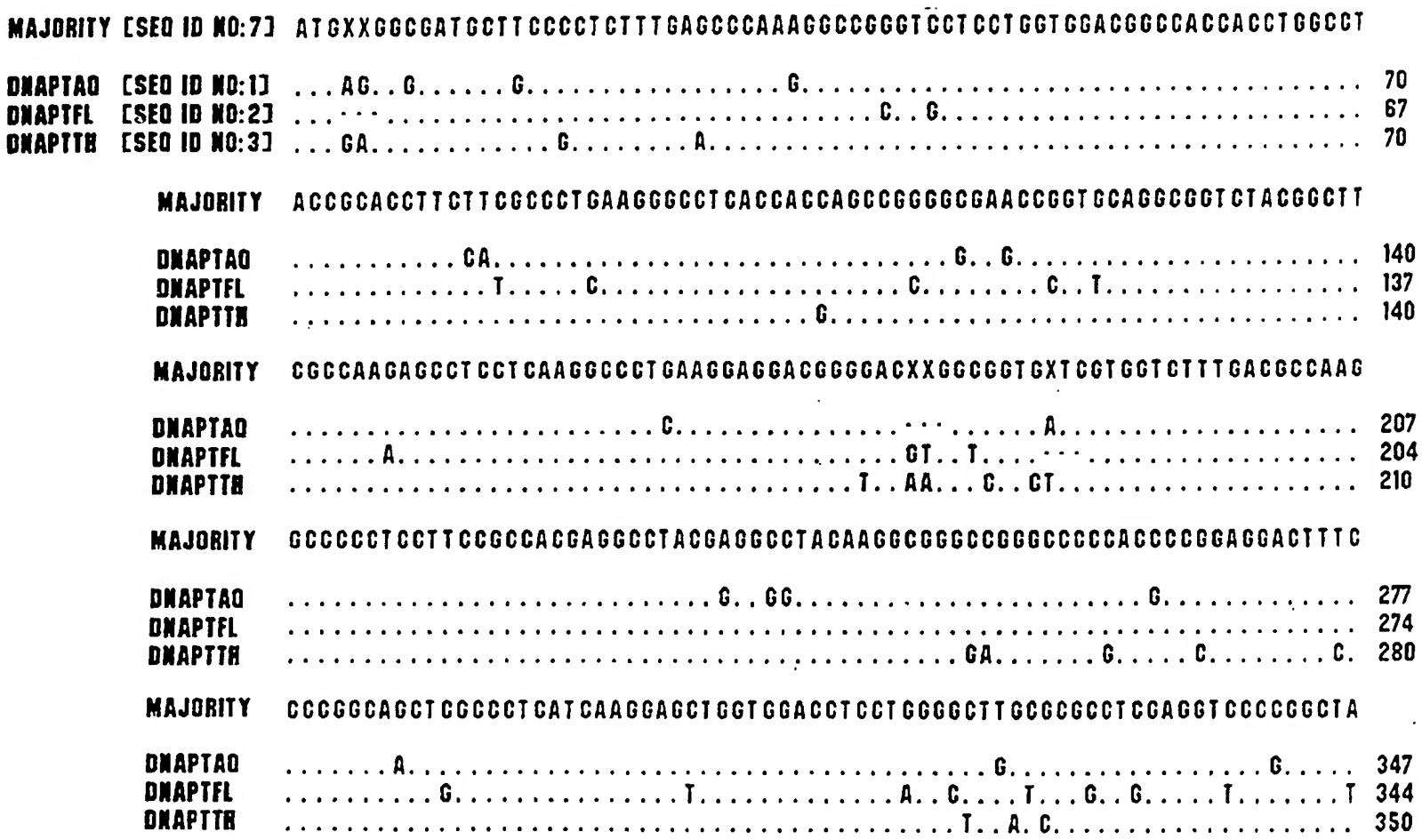

MAJORITY [SEQ ID NO:7] ATGXXGGCGATGCTTCCCCTCTTTGAGCCCAAAGGCCGGGTCCTCCTGGTGGACGGCCACCACCTGGCCT
DNAPTAQ [SEQ ID NO:1] ...AG..G.....G.....G..... 70
DNAPTFL [SEQ ID NO:2] .....C..G..... 67
DNAPTTH [SEQ ID NO:3] ...GA.....G.....A..... 70
MAJORITY ACCGCACCTTCTTCGCCCTGAAGGGCCTCACCACCAGCCGGGGCGAACCGGTGCAGGCGGTCTACGGCTT
DNAPTAQ .....CA.....G..G..... 140
DNAPTFL .....T.....C.....C.....C..T..... 137
DNAPTTH .....G..... 140
MAJORITY CGCCAAGAGCCTCCTCAAGGCCCTGAAGGAGGACGGGGACXXGGCGGTGXTCGTGGTCTTTGACGCCAAG
DNAPTAQ .....C.....A..... 207
DNAPTFL .....A.....GT..T..... 204
DNAPTTH .....T..AA...C..CT..... 210
MAJORITY GCCCCCTCCTTCCGCCACGAGGCCTACGAGGCCTACAAGGCGGGCCGGGCCCCCACCCCGGAGGACTTTC
DNAPTAQ .....G..GG.....G..... 277
DNAPTFL 274
DNAPTTH .....GA.....G.....C.....C. 280
MAJORITY CCCGGCAGCTCGCCCTCATCAAGGAGCTGGTGGACCTCCTGGGGCTTGCGCGCCTCGAGGTCCCCGGCTA
DNAPTAQ .....A.....G.....G..... 347
DNAPTFL .....G.....T.....A..C....T...G..G.....T.....T 344
DNAPTTH .....T..A.C..... 350

FIG. 2B

```
MAJORITY [SEQ ID NO:7] CGAGGCGGACGACGTXCTGGCCACCCTGGCCAAGAAGGCGGAAAAGGAGGGGTACGAGGTGCGCATCCTC

DNAPTAQ  [SEQ ID NO:1] ..............C.......G.............................C........C.........  417
DNAPTFL  [SEQ ID NO:2] T.............G.................CG.................................  414
DNAPTTH  [SEQ ID NO:3] ..............T..C.....................................................  420

MAJORITY ACCGCCGACCGCGACCTCTACCAGCTCCTTTCCGACCGCATCGCCGTCCTCCACCCCGAGGGGTACCTCA

DNAPTAQ  .........AAA.....T.........................CA.............................  487
DNAPTFL  ..T.............................G..G.........A..........T...........G.  484
DNAPTTH  ........................A...G.C.........G.....................CC......  490

MAJORITY TCACCCCGGCGTGGCTTTGGGAGAAGTACGGCCTGAGGCCGGAGCAGTGGGTGGACTACCGGCCCCTGGC

DNAPTAQ  ..........C...........A.................C..C.......CC................A.  557
DNAPTFL  ..................AC..............C.C.................................  554
DNAPTTH  .........A.........................C.....................T...C.....C.T  560

MAJORITY GGGGGACCCCTCCGACAACCTCCCCGGGGTCAAGGGCATCGGGGAGAAGACCGCCCXGAAGCTCCTCXAG

DNAPTAQ  C......GAG...........T.............................G..GAG......T..GG..  627
DNAPTFL  ............G..T...A.........G.....................A..G....A..CGC.  624
DNAPTTH  ..........................................................TC.........A..  630

MAJORITY GAGTGGGGGAGCCTGGAAAACCTCCTCAAGAACCTGGACCGGGTGAAGCCCGC···CXTCCGGGACAAGA

DNAPTAQ  ..................GC.....................C.............···A.............  694
DNAPTFL  .......................T..C..C.........A..........T.···.T.G.........C  691
DNAPTTH  ........A.....................................A.....A.AAAA.G.............  700
```

FIG. 2C


MAJORITY [SEQ ID NO:7] TCCAGGCCCACATGGAXGACCTGAXGCTCTCCTGGGAGCTXTCCCAGGTGCGCACCGACCTGCCCCTGGA
DNAPTAQ [SEQ ID NO:1] ...T.....C..T....A.....C..GG..A..... 764
DNAPTFL [SEQ ID NO:2] .....GGG.....G.C....GCC..T...C..A....T.....A...T..... 761
DNAPTTH [SEQ ID NO:3] ..A.....C....A.....C.G.....T.....C....G.....C..... 770
MAJORITY GGTGGACTTCGCCAAGXGGCGGGAGCCCGACCGGGAGGGGCTTAGGGCCTTTCTGGAGAGGCTGGAGTTT
DNAPTAQ .....AA.....A.....T..... 834
DNAPTFL .....GG.G.C.C..CACA...A...T.....T..GC....T...T.....C..T..... 831
DNAPTTH .....C.....C..G.....C.....C 840
MAJORITY GGCAGCCTCCTCCACGAGTTCGGCCTCCTGGAGGGCCCCAAGGCCCTGGAGGAGGCCCCCTGGCCCCCGC
DNAPTAQ .....T.....AA..... 904
DNAPTFL ..A.....G..G.....GGCA.....T. 901
DNAPTTH .....C....GCCC..... 910
MAJORITY CGGAAGGGGCCTTCGTGGGCTTTGTCCTTTCCCGCCCCGAGCCCATGTGGGCCGAGCTTCTGGCCCTGGC
DNAPTAQ .....G.....AAG.....T..... 974
DNAPTFL .....T..TT.....TC.T.....T..... 971
DNAPTTH .....C.....C.....G.....AAA..... 980
MAJORITY CGCCGCCAGGGAGGGCCGGGTCCACCGGGCACCAGACCCCTTTAXGGGCCTXAGGGACCTXAAGGAGGTG
DNAPTAQ .....G.....C..C..G..T.A..AA.C...C.....G.....C. 1044
DNAPTFL T.GG..GT.....G..CC....T.....A.....C...G.....G.....T....G.... 1041
DNAPTTH ....TG.....C.....G.....G.....GGC...G..A.A.....C.....C 1050

FIG. 2D

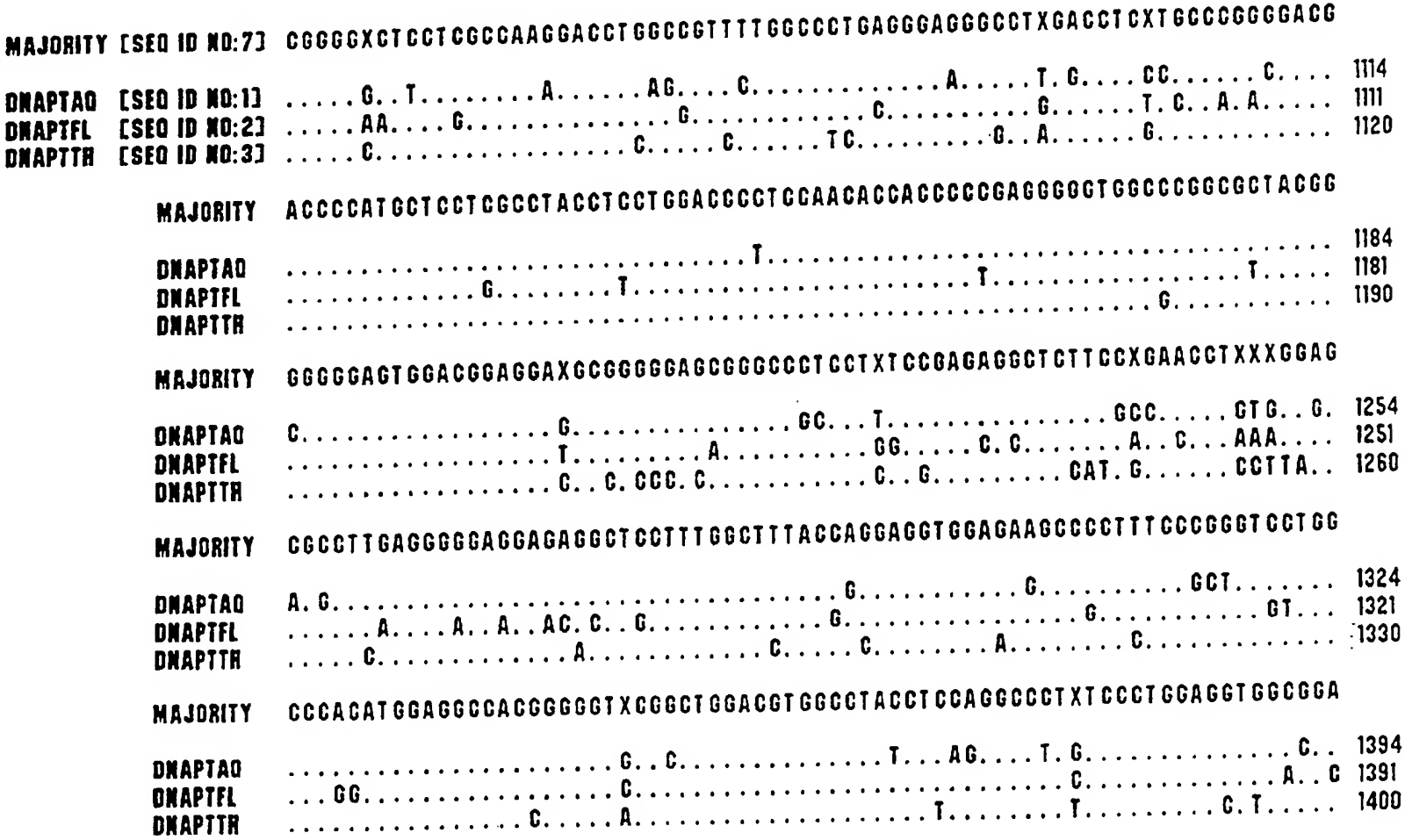

MAJORITY [SEQ ID NO:7] CGGGGXCTCCTCGCCAAGGACCTGGCCGTTTTGGCCCTGAGGGAGGGCCTXGACCTCXTGCCCGGGGACG
DNAPTAQ [SEQ ID NO:1] .....G..T.....A.....AG....C.....A.....T.G....CC.....C.... 1114
DNAPTFL [SEQ ID NO:2] .....AA....G.....G.....C.....G.....T.C..A.A..... 1111
DNAPTTH [SEQ ID NO:3] .....C.....C.....C.....TC.....G..A.....G..... 1120
MAJORITY ACCCCATGCTCCTCGCCTACCTCCTGGACCCCTCCAACACCACCCCCGAGGGGCTGGCCCGGCGCTACGG
1184
DNAPTAQ .....T..... 1181
DNAPTFL .....G.....T.....T.....T..... 1190
DNAPTTH .....G.....
MAJORITY GGGGGAGTGGACGGAGGAXGCGGGGGAGCGGGCCCTCCTXTCCGAGAGGCTCTTCCXGAACCTXXXGGAG
1254
DNAPTAQ C.....G.....GC...T.....GCC.....GTG..G. 1251
DNAPTFL .....T.....A.....GG.....C.C.....A..C...AAA.... 1260
DNAPTTH .....C..C.CCC.C.....C..G.....CAT.G.....CCTTA..
MAJORITY CGCCTTGAGGGGGAGGAGAGGCTCCTTTGGCTTTACCAGGAGGTGGAGAAGCCCCTTTCCCGGGTCCTGG
1324
DNAPTAQ A.G.....G.....G.....GCT..... 1321
DNAPTFL .....A....A..A..AC.C..G.....G.....G.....GT... 1330
DNAPTTH .....C.....A.....C.....C.....A.....C.....
MAJORITY CCCACATGGAGGCCACGGGGGTXCGGCTGGACGTGGCCTACCTCCAGGCCCTXTCCCTGGAGGTGGCGGA
1394
DNAPTAQ .....G..C.....T...AG....T.G.....C.. 1391
DNAPTFL ...GG.....C.....C.....A..C 1400
DNAPTTH .....C.....A.....T.....T.....C.T.....

FIG. 2E

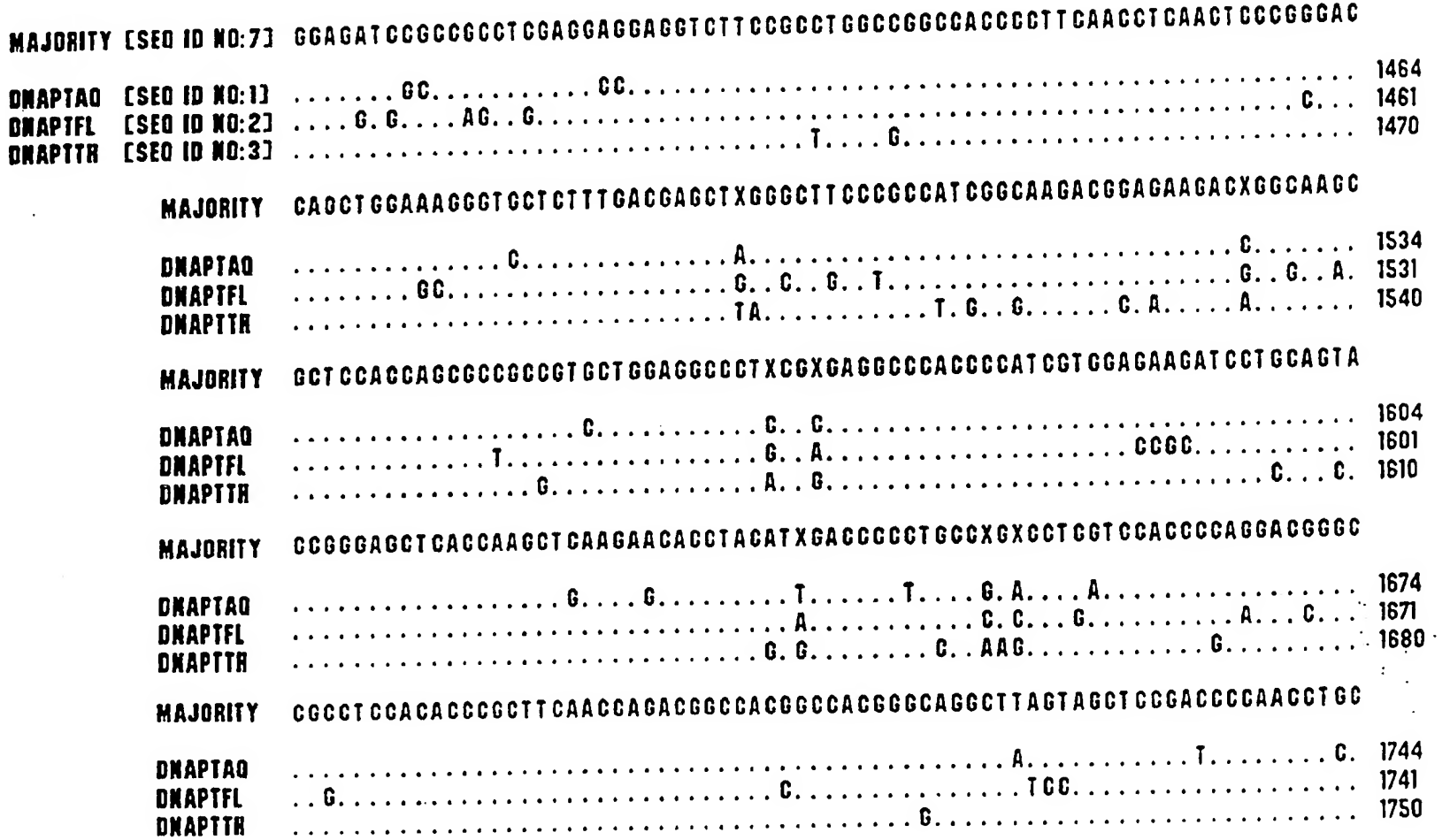

MAJORITY [SEQ ID NO:7] GGAGATCCGCCGCCTCGAGGAGGAGGTCTTCCGCCTGGCCGGCCACCCCTTCAACCTCAACTCCCGGGAC
DNAPTAQ [SEQ ID NO:1] 1464
DNAPTFL [SEQ ID NO:2] 1461
DNAPTTR [SEQ ID NO:3] 1470
MAJORITY CAGCTGGAAAGCGTGCTCTTTGACGAGCTXGGGCTTCCCGCCATCGGCAAGACGGAGAAGACXGGCAAGC
DNAPTAQ 1534
DNAPTFL 1531
DNAPTTR 1540
MAJORITY GCTCCACCAGCGCCGCCGTGCTGGAGGCCCTXCGXGAGGCCCACCCCATCGTGGAGAAGATCCTGCAGTA
DNAPTAQ 1604
DNAPTFL 1601
DNAPTTR 1610
MAJORITY CCGGGAGCTCACCAAGCTCAAGAACACCTACATXGACCCCCTGCCXGXCCTCGTCCACCCCAGGACGGGC
DNAPTAQ 1674
DNAPTFL 1671
DNAPTTR 1680
MAJORITY CGCCTCCACACCCGCTTCAACCAGACGGCCACGGCCACGGGCAGGCTTAGTAGCTCCGACCCCAACCTGC
DNAPTAQ 1744
DNAPTFL 1741
DNAPTTR 1750

FIG. 2F


MAJORITY [SEQ ID NO:7] AGAACATCCCCGTCCGCACCCCXCTGGGCCAGAGGATCCGCCGGGCCTTCGTGGCCGAGGAGGGXTGGGT
DNAPTAQ [SEQ ID NO:1] ..... G..T..G..... A.C..... G...C. 1814
DNAPTFL [SEQ ID NO:2] ..... G..... T..... C.C..... A..... C..... 1811
DNAPTTH [SEQ ID NO:3] ..... CT..... C...T....C 1820
MAJORITY GTTGGTGGCCCTGGACTATAGCCAGATAGAGCTCCGGGTCCTGGCCCACCTCTCCGGGGACGAGAACCTG
DNAPTAQ A..... A....C..... C..... 1884
DNAPTFL .C.....T.T.....C.....T.....T..... 1881
DNAPTTH ..... C.....C..... A..... 1890
MAJORITY ATCCGGGTCTTCCAGGAGGGGAGGGACATCCACACCCAGACCGCCAGCTGGATGTTCGGCGTCCCCCCGG
DNAPTAQ ..... C..... GG..... G.. 1954
DNAPTFL ..... T..... TT....C. 1951
DNAPTTH ...A..... A..... A..... 1960
MAJORITY AGGCCGTGGACCCCCTGATGCGCCGGGCGGCCAAGACCATCAACTTCGGGGTCCTCTACGGCATGTCCGC
DNAPTAQ ..... G.. 2024
DNAPTFL .A.GG..A.....T..... G..... 2021
DNAPTTH ..... GG.G..... C..... 2030
MAJORITY CCACCGCCTCTCCCAGGAGCTTGCCATCCCCTACGAGGAGGCGGTGGCCTTCATTGAGCGCTACTTCCAG
DNAPTAQ ..... A..... T..... CCA..... T... 2094
DNAPTFL ..... GG..... T..... 2091
DNAPTTH ...TA.G..... T..A..... A 2100

FIG. 2G

```
MAJORITY [SEQ ID NO:7] AGCTTCCCCAAGGTGCGGGCCTGGATTGAGAAGACCCTGGAGGAGGGCAGGACGCCGGGGTACGTGGAGA

DNAPTAQ  [SEQ ID NO:1] ..................................................................... 2164
DNAPTFL [SEQ ID NO:2] ....A.....................GG.....C.........C.CC.........T..... 2161
DNAPTTH [SEQ ID NO:3] ...........................A..A.................G....A.....C.....A. 2170

MAJORITY CCCTCTTCGGCCGCCGGCGCTACGTGCCCGACCTCAACGCCCGGGTGAAGAGCGTGCGGGAGGCGGCGGA

DNAPTAQ  ................C..........A.....AG.G.............................C.. 2234
DNAPTFL  ....................T.................................C.......... 2231
DNAPTTH  ..........AA.AA.....................................CA.....C..... 2240

MAJORITY GCGCATGGCCTTCAACATGCCCGTCCAGGGCACCGCCGCCGACCTCATGAAGCTGGCCATGGTGAAGCTC

DNAPTAQ  ..........................................................T.......... 2304
DNAPTFL  ....................G.....................................CG...T 2301
DNAPTTH  ..............................................C.............. 2310

MAJORITY TTCCCCCGGCTXCAGGAAATGGGGGCCAGGATGCTCCTXCAGGTCCACGACGAGCTGGTCCTCGAGGCCC

DNAPTAQ  ......A....GG.....................T.............................. 2374
DNAPTFL  ..........T......C.......G........TT.G.....G..................... 2371
DNAPTTH  ........C..C.G...G.........C.C........C.................CC....G..... 2380

MAJORITY CCAAAGAGCGGGCGGAGGXGGTGGCCGCTTTGGCCAAGGAGGTCATGGAGGGGGTCTATCCCCTGGCCGT

DNAPTAQ  .A......A.........CC......CGGC.....................G.............. 2444
DNAPTFL  ....G..C.........AG...A.....................................GG......CAG.. 2441
DNAPTTH  ..C...C......C....A......G................C.......AA..C.........C..... 2450
```

FIG. 2H

```
MAJORITY [SEQ ID NO:7]  GCCCCTGGAGGTGGAGGTGGGGATGGGGGAGGACTCGCTCTCCGCCAAGGAGTAG

DNAPTAQ  [SEQ ID NO:1]  ........................A.............................GA
DNAPTFL  [SEQ ID NO:2]  ......................CC.................................
DNAPTTH  [SEQ ID NO:3]  ..................................T..........GT...
```

FIG. 3A

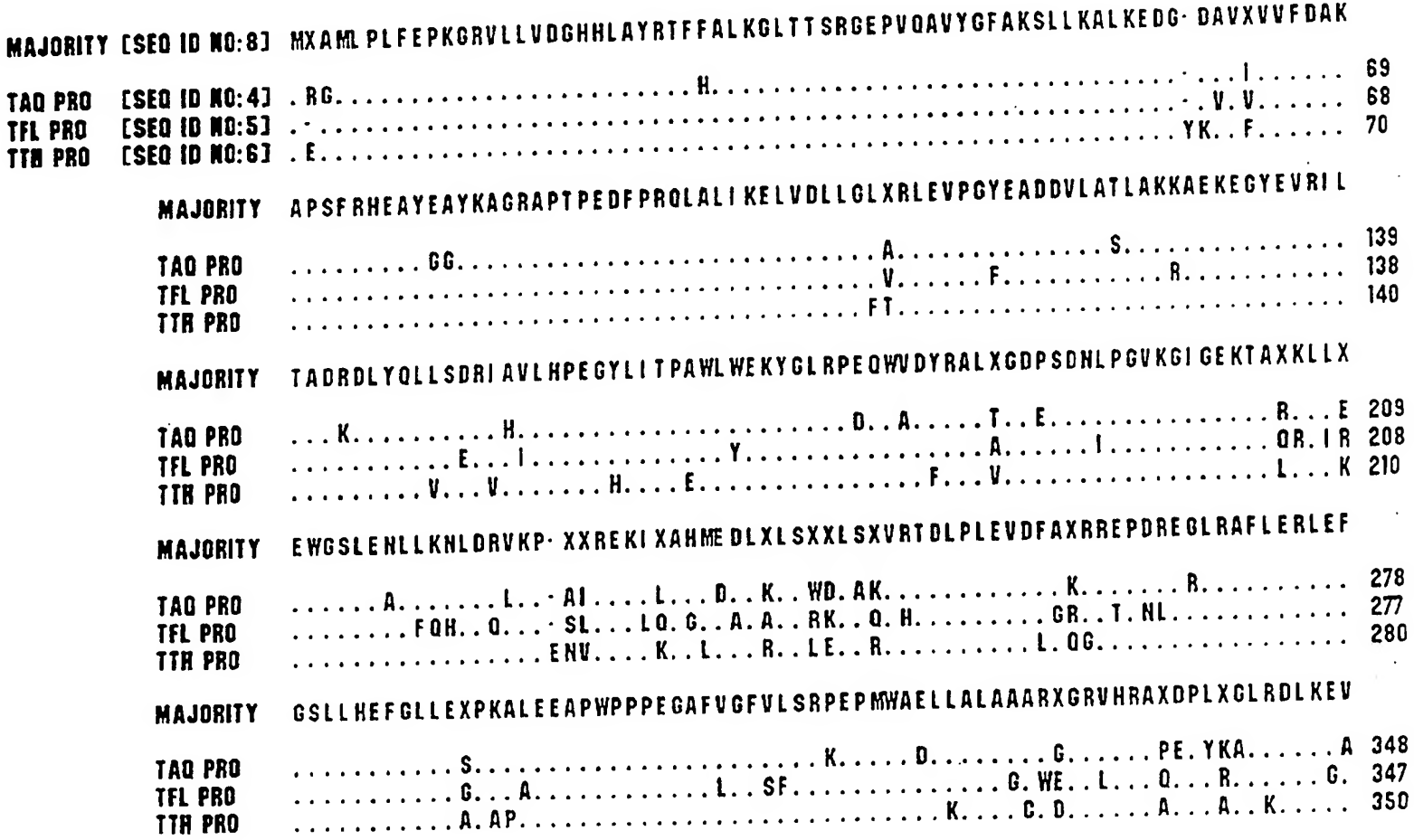

MAJORITY [SEQ ID NO:8] MXAML PLFEPKGRVLLVDGHHLAYRTFFALKGLTTSRGEPVQAVYGFAKSLLKALKEDG· DAVXVVFDAK
TAQ PRO [SEQ ID NO:4] .RG.....H.....I..... 69
TFL PRO [SEQ ID NO:5] .-.....V.V..... 68
TTH PRO [SEQ ID NO:6] .E.....YK..F..... 70
MAJORITY APSFRHEAYEAYKAGRAPTPEDFPRQLALIKELVDLLGLXRLEVPGYEADDVLATLAKKAEKEGYEVRIL
TAQ PRO .....GG.....A.....S..... 139
TFL PRO .....V.....F.....R..... 138
TTH PRO .....FT..... 140
MAJORITY TADRDLYQLLSDRIAVLHPEGYLITPAWLWEKYGLRPEQWVDYRALXGDPSDNLPGVKGIGEKTAXKLLX
TAQ PRO ...K.....H.....D..A.....T..E.....R...E 209
TFL PRO .....E...I.....Y.....A.....I.....QR.IR 208
TTH PRO .....V...V.....H....E.....F...V.....L...K 210
MAJORITY EWGSLENLLKNLDRVKP·XXREKIXAHMEDLXLSXXLSXVRTDLPLEVDFAXRREPDREGLRAFLERLEF
TAQ PRO .....A.....L..·AI....L...D..K..WD.AK.....K.....R..... 278
TFL PRO .....FQH..Q...·SL...LQ.G..A.A..RK..Q.H.....GR..T.NL..... 277
TTH PRO .....ENV....K..L...R..LE..R.....L.QG..... 280
MAJORITY GSLLHEFGLLEXPKALEEAPWPPPEGAFVGFVLSRPEPMWAELLALAAARXGRVHRAXDPLXGLRDLKEV
TAQ PRO .....S.....K.....D.....G.....PE.YKA.....A 348
TFL PRO .....G...A.....L..SF.....G.WE..L...Q...R.....G. 347
TTH PRO .....A.AP.....K....C.D.....A...A..K..... 350

FIG. 3B

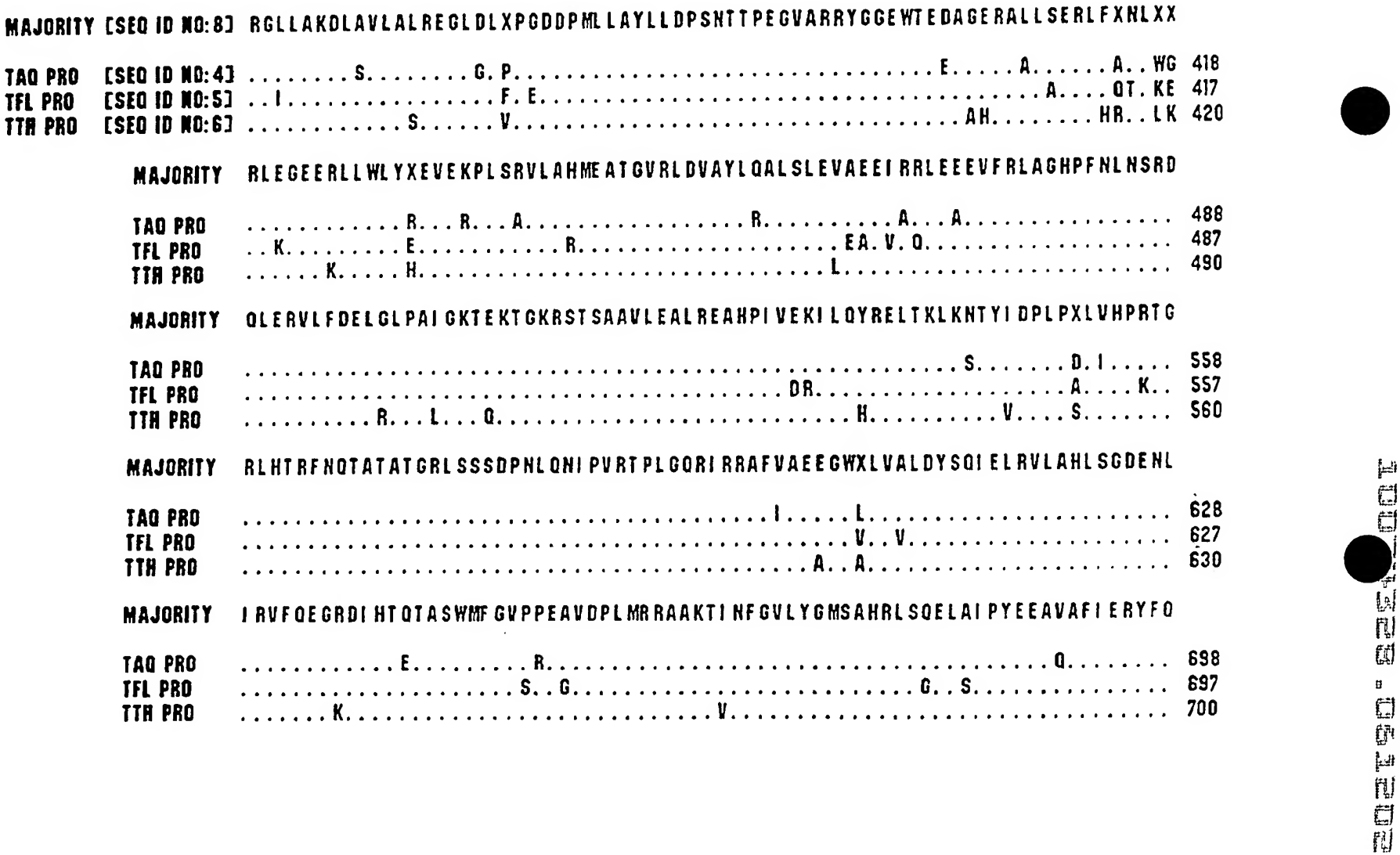
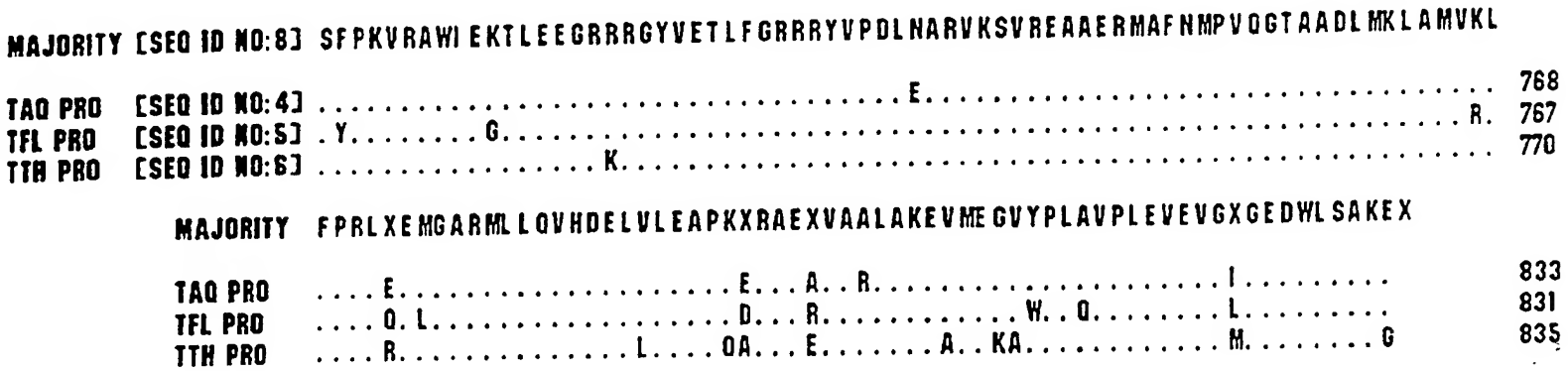

MAJORITY [SEQ ID NO:8] RGLLAKDLAVLALREGLDLXPGDDPMLLAYLLDPSNTTPEGVARRYGGEWTEDAGERALLSERLFXNLXX
TAQ PRO [SEQ ID NO:4] .....S.....G.P.....E.....A.....A..WG 418
TFL PRO [SEQ ID NO:5] ..I.....F.E.....A....QT.KE 417
TTH PRO [SEQ ID NO:6] .....S.....V.....AH.....HR..LK 420
MAJORITY RLEGEERLLWLYXEVEKPLSRVLAHMEATGVRLDVAYLQALSLEVAEEIRRLEEEVFRLAGHPFNLNSRD
TAQ PRO .....R...R...A.....R.....A...A..... 488
TFL PRO ..K.....E.....R.....EA.V.Q..... 487
TTH PRO .....K.....H.....L..... 490
MAJORITY QLERVLFDELGLPAIGKTEKTGKRSTSAAVLEALREAHPIVEKILQYRELTKLKNTYIDPLPXLVHPRTG
TAQ PRO .....S.....D.I..... 558
TFL PRO .....DR.....A....K.. 557
TTH PRO .....R...L...Q.....H.....V....S..... 560
MAJORITY RLHTRFNQTATATGRLSSSDPNLQNIPVRTPLGQRIRRAFVAEEGWXLVALDYSQIELRVLAHLSGDENL
TAQ PRO .....I.....L..... 628
TFL PRO .....V..V..... 627
TTH PRO .....A..A..... 630
MAJORITY IRVFQEGRDIHTQTASWMFGVPPEAVDPLMRRAAKTINFGVLYGMSAHRLSQELAIPYEEAVAFIERYFQ
TAQ PRO .....E.....R.....Q..... 698
TFL PRO .....S..G.....G..S..... 697
TTH PRO .....K.....V..... 700

FIG. 3C


MAJORITY [SEQ ID NO:8] SFPKVRAWIEKTLEEGRRRGYVETLFGRRRYVPDLNARVKSVREAAERMAFNMPVQGTAADLMKLAMVKL
TAQ PRO [SEQ ID NO:4] 768
TFL PRO [SEQ ID NO:5] 767
TTH PRO [SEQ ID NO:6] 770
MAJORITY FPRLXEMGARMLLQVHDELVLEAPKXRAEXVAALAKEVMEGVYPLAVPLEVEVGXGEDWLSAKEX
TAQ PRO 833
TFL PRO 831
TTH PRO 835

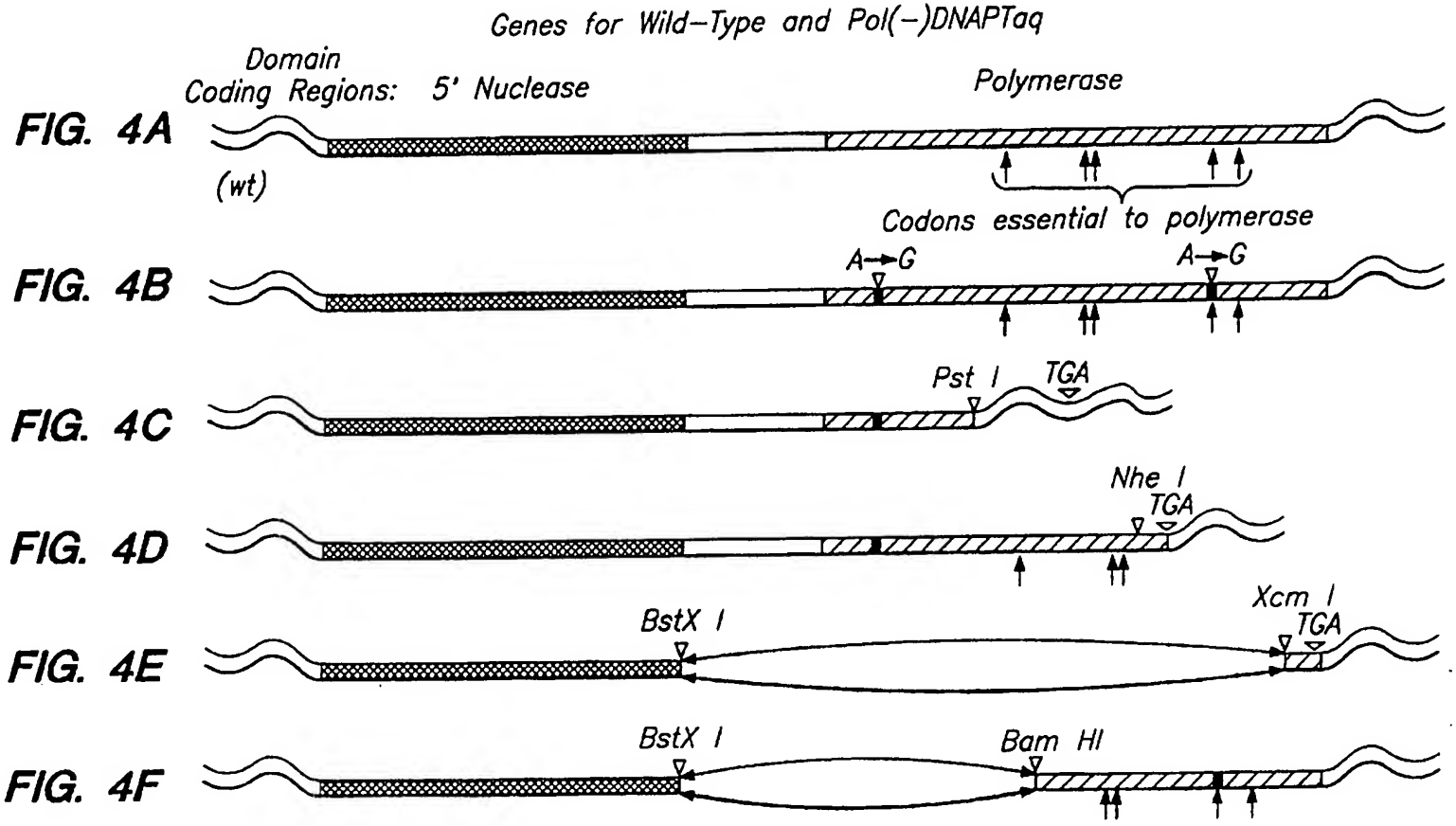


FIG. 4A

FIG. 4B

FIG. 4C

FIG. 4D

FIG. 4E

FIG. 4F

Genes for Wild-Type and Pol(-) DNAPTfl

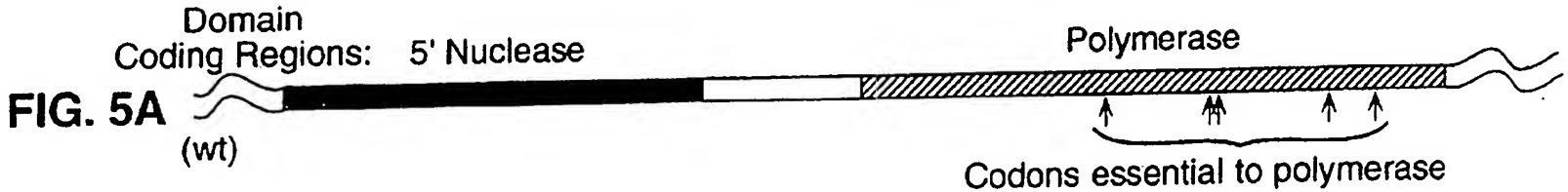


FIG. 5A

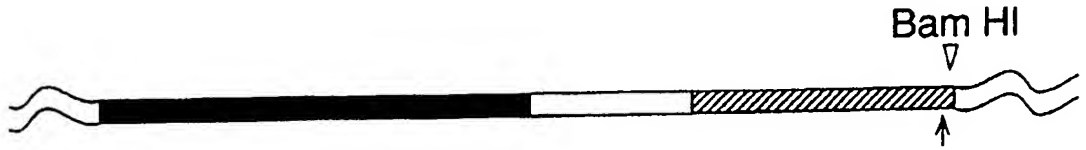


FIG. 5B

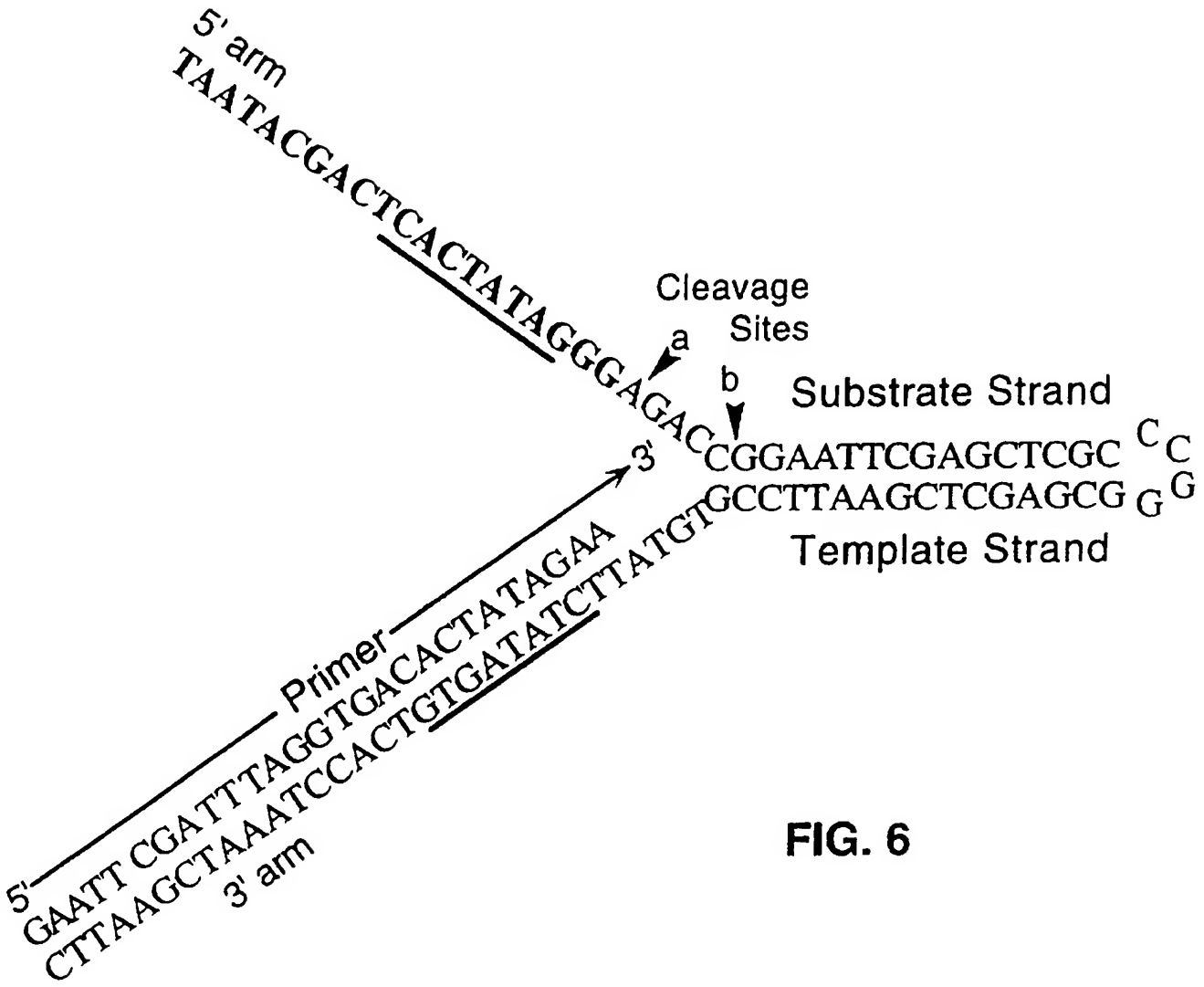

5' arm
TAATACGACTCACTATAGGGAGAC
Cleavage
Sites
a
b
Substrate Strand
3'
CGGAATTCGAGCTCGC C C
GCCTTAAGCTCGAGCG G G
Template Strand
Primer
5'
GAATT CGATTTAGGTGACACTATAGAA
CTTAAGCTAAATCCACTGTGATATCTTATGT
3' arm

FIG. 6

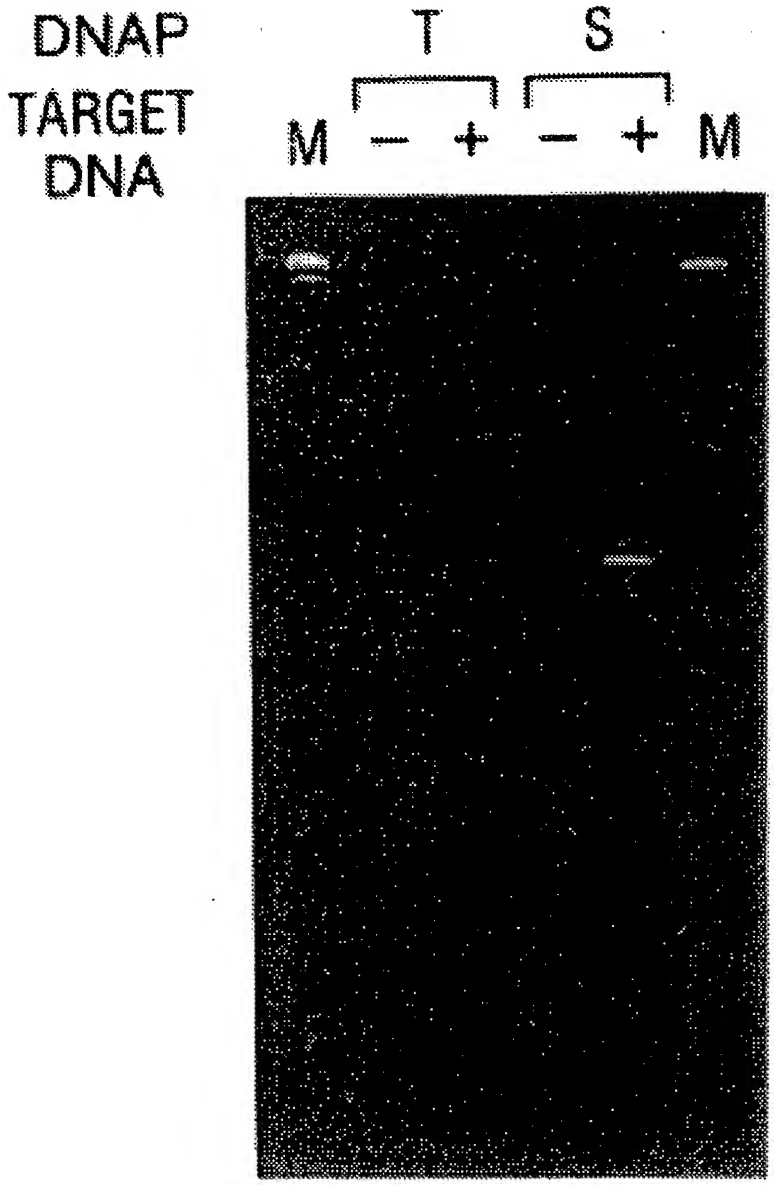


FIG. 7

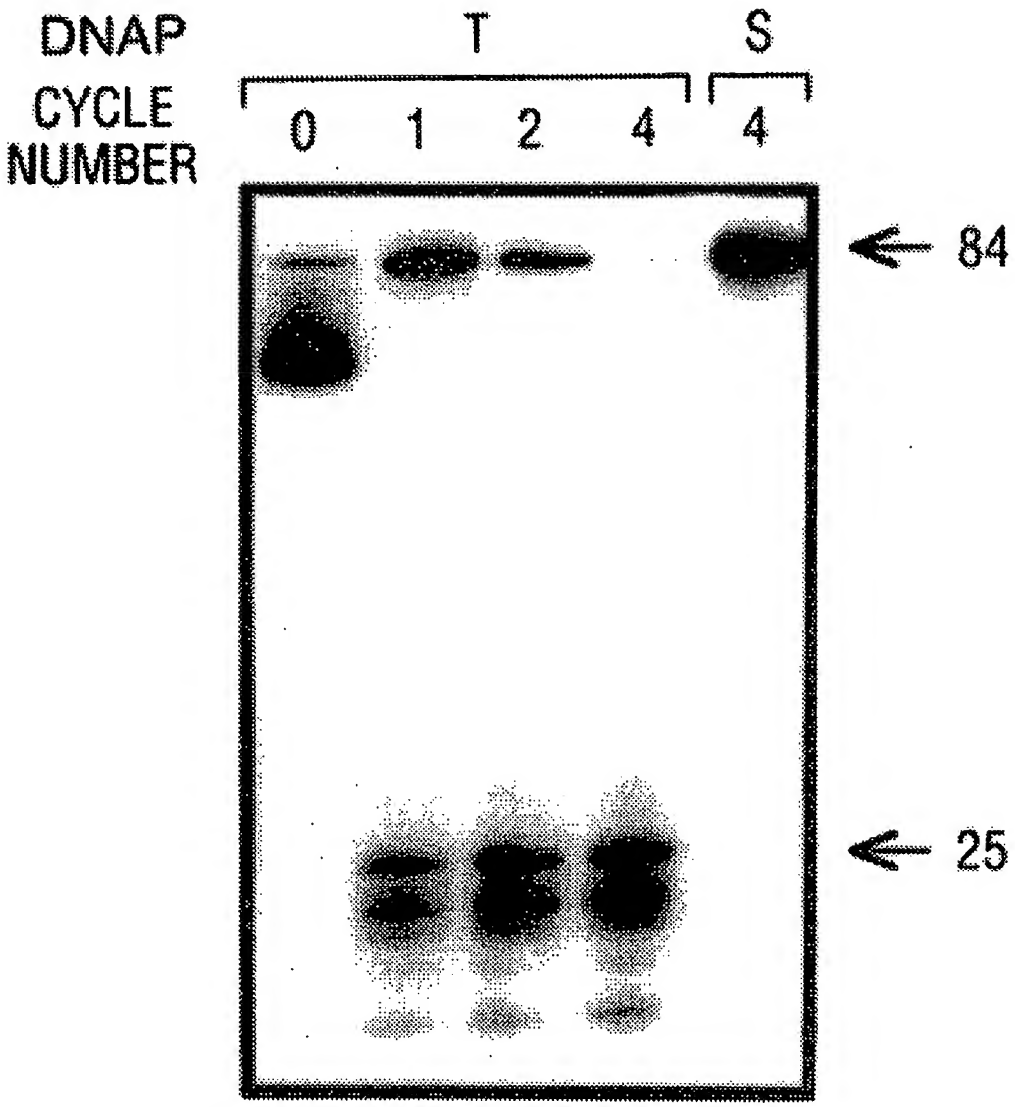


FIG. 8

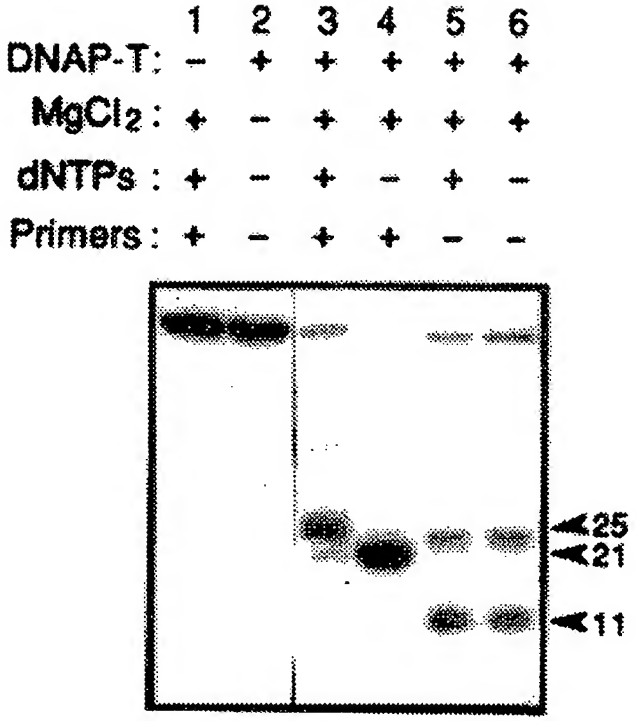


FIG. 9A

FIG. 9B

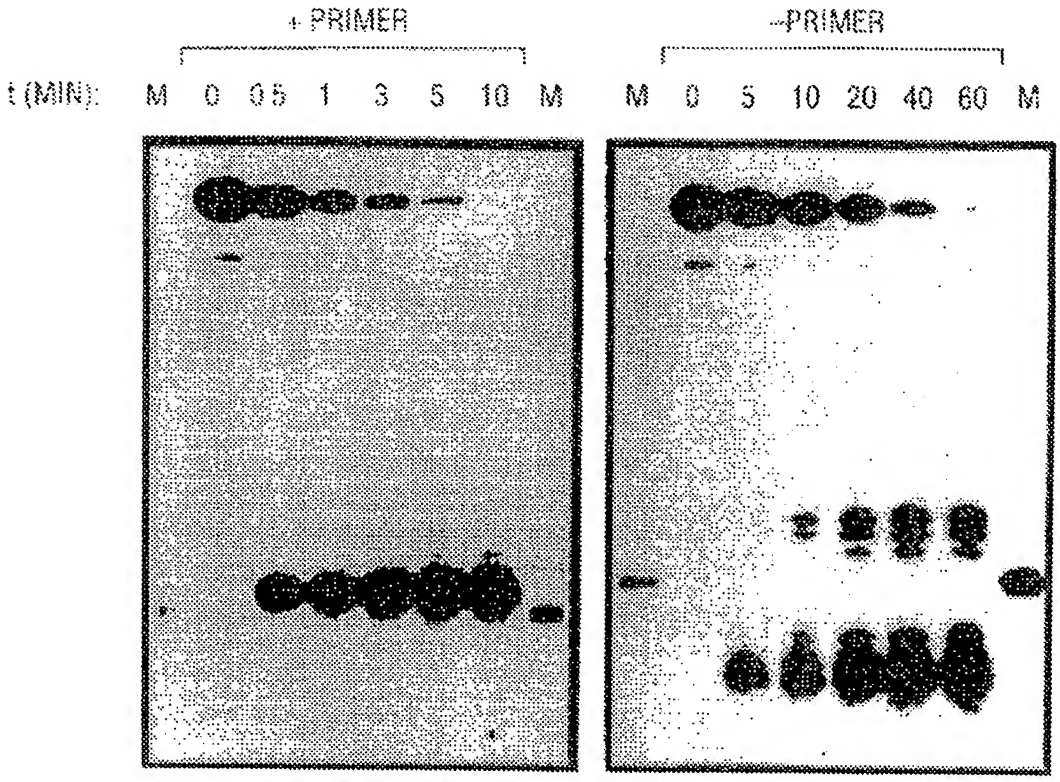


FIG. 10A

FIG. 10B

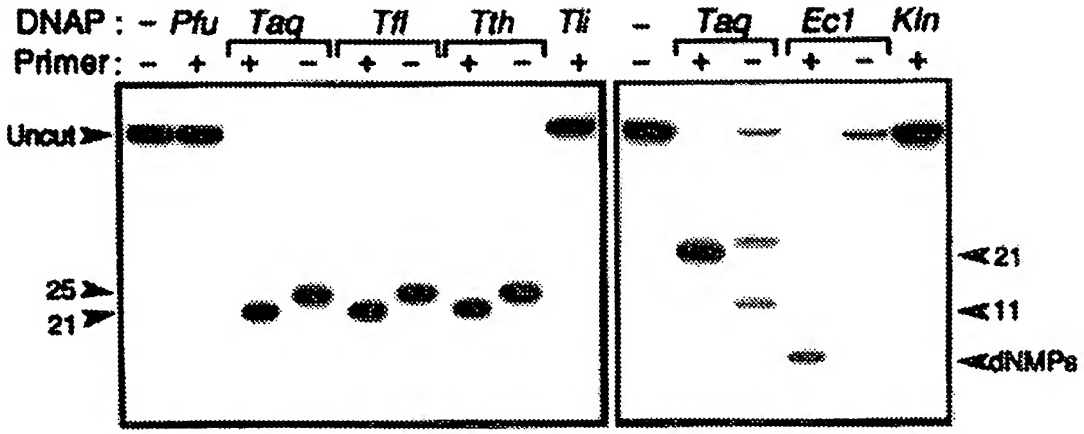
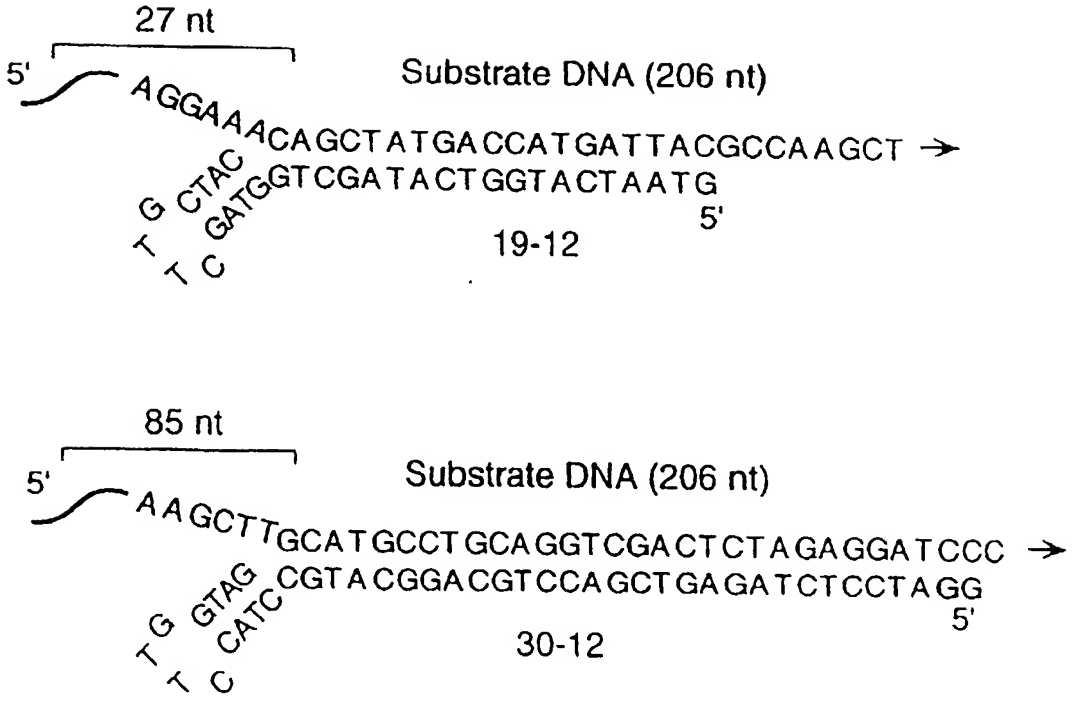


FIG. 11A

FIG. 11B

FIG. 12A


27 nt
5'
Substrate DNA (206 nt)
AGGAAACAGCTATGACCATGATTACGCCAAGCT
GATGGTCGATACTGGTACTAATG
5'
19-12
85 nt
5'
Substrate DNA (206 nt)
AAGCTTGCATGCCTGCAGGTCGACTCTAGAGGATCCC
CGTACGGACGTCCAGCTGAGATCTCCTAGG
5'
30-12

15 nt

Substrate RNA (46 nt)

5' ~ AAGCUUGCAUGCCUGCAGGUCGACUCUAGAGGAUCCCC 3'

3' CGTACGGACGTCCAGCTGAGATCTCCTAGG 5'

30-0

FIG. 13A

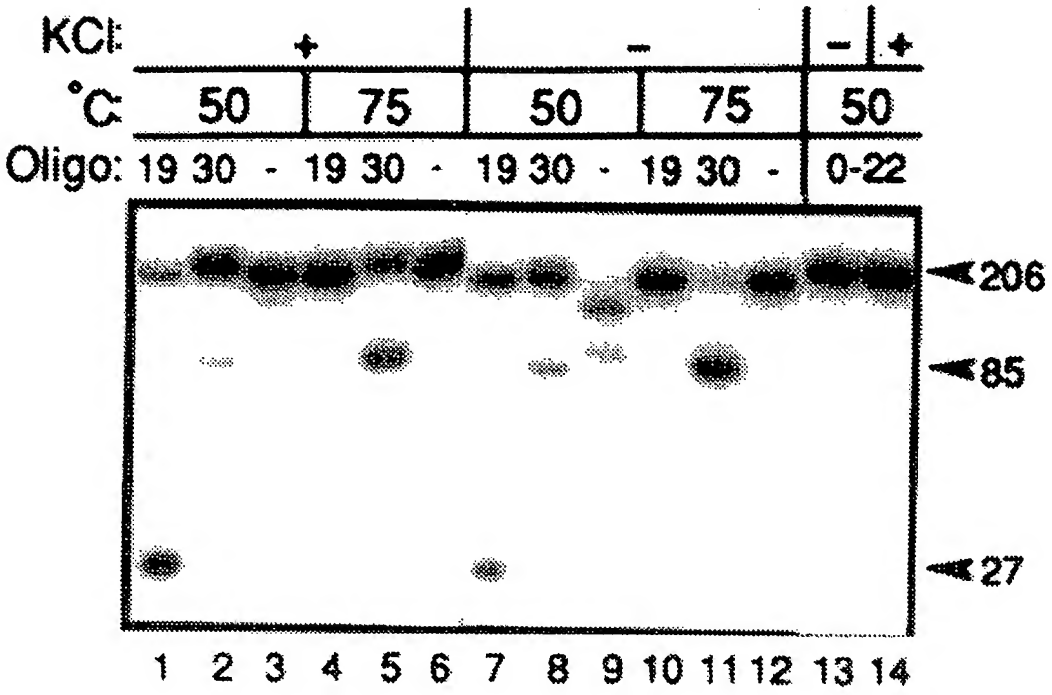


FIG. 12B

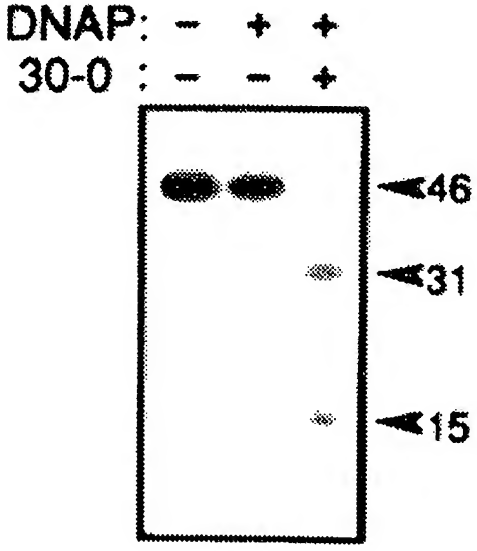


FIG. 13B

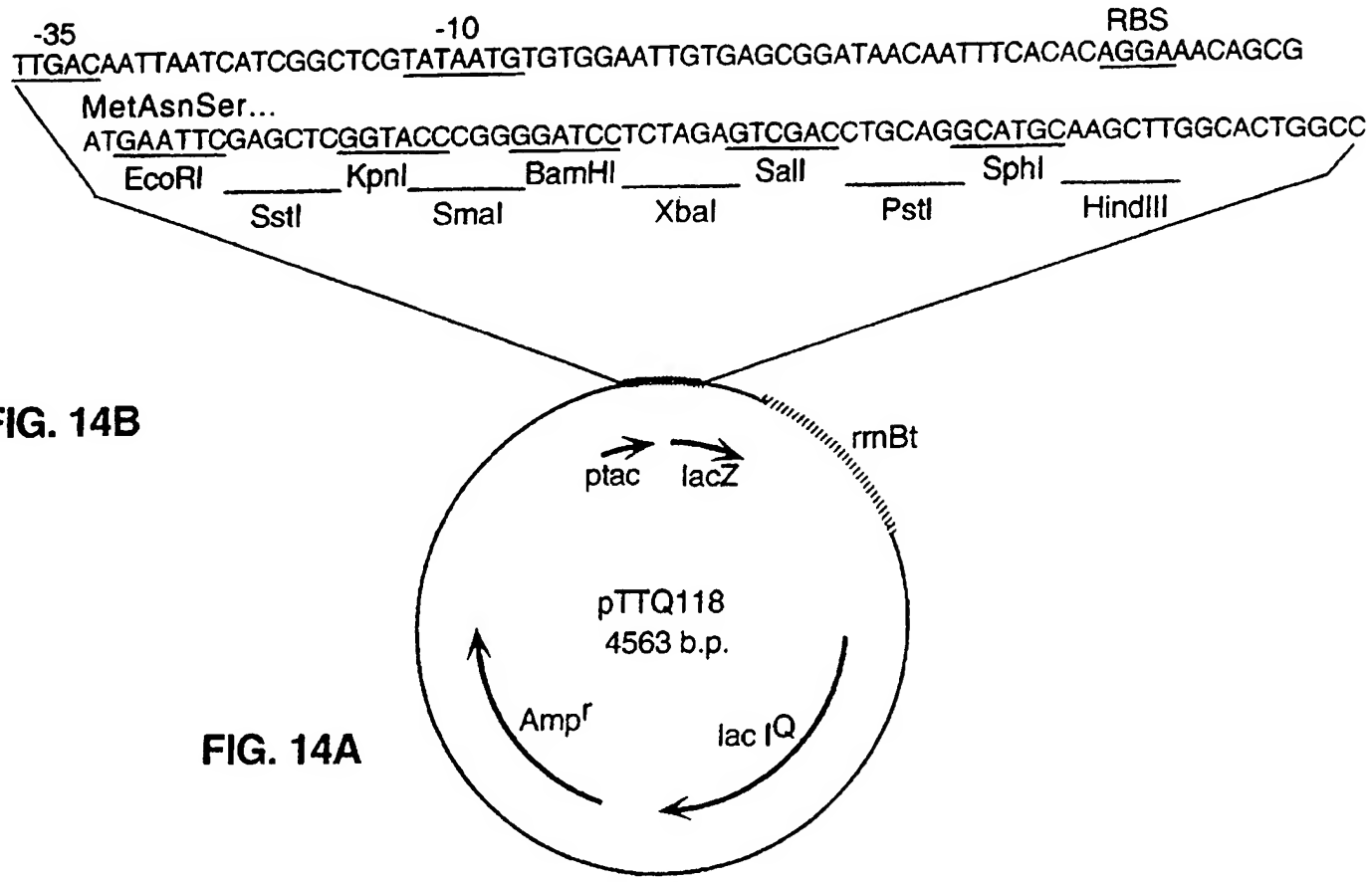


FIG. 14B

FIG. 14A

FIG. 14C

RBS: Ribosome binding site
ptac: Synthetic tac promoter
lac I^Q: Lac repressor gene

lacZ: Beta-galactosidase alpha fragment
rrnBt: E. coli rrnB transcription terminator

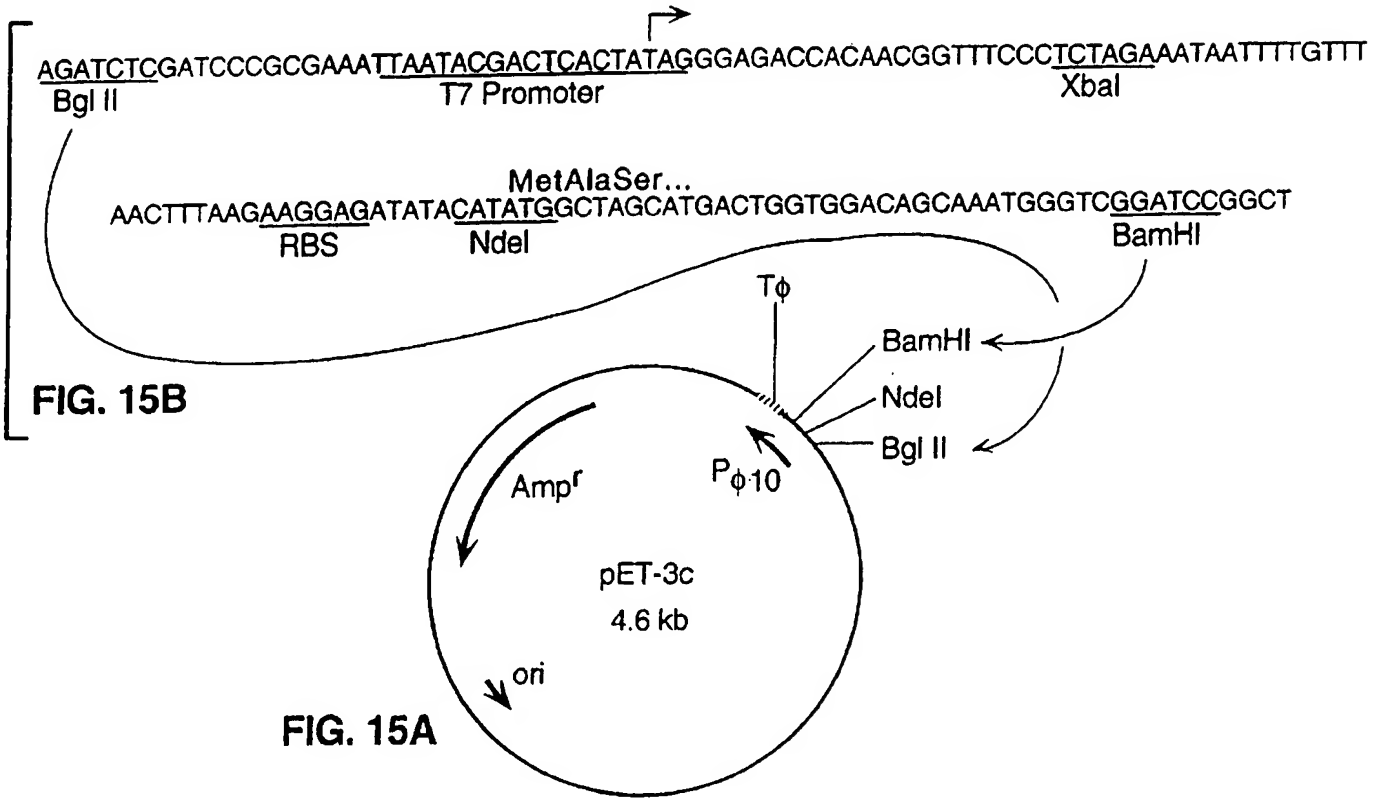


FIG. 15B

FIG. 15A

$P_{\phi 10}$: Bacteriophage T7 ϕ10 promoter RBS: Ribosome binding site

Tϕ: T7 ϕ Terminator

FIG. 15C

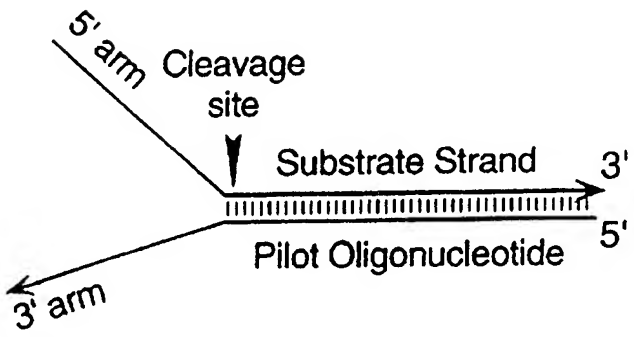


FIG. 16A

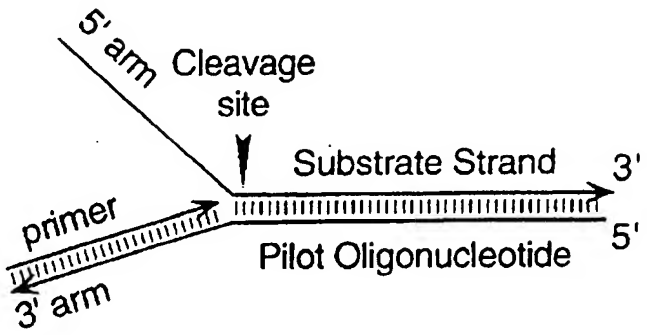


FIG. 16B

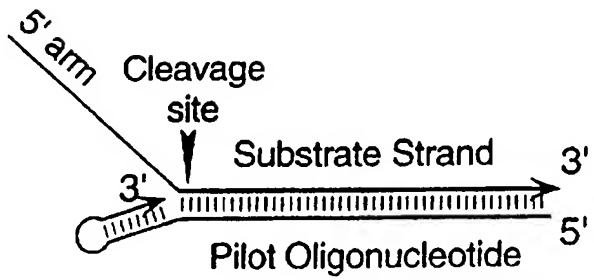


FIG. 16C

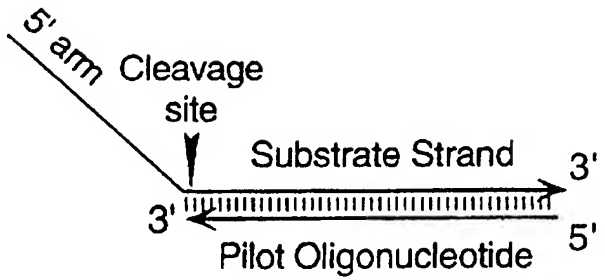


FIG. 16D

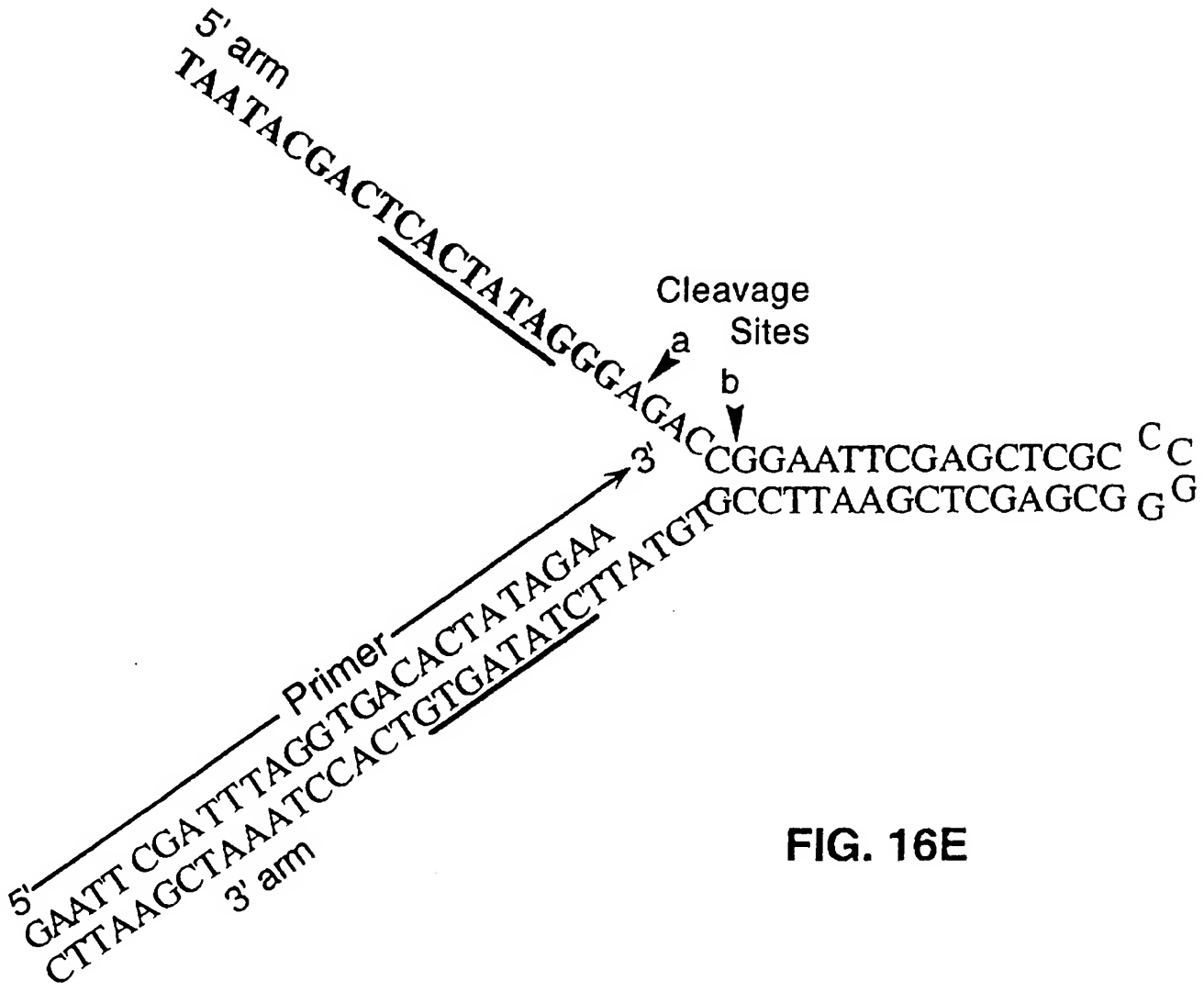

5' arm
TAATACGACTCACTATAGGGAGACC
Cleavage
Sites
a
b
3'
CGGAATTCGAGCTCGC C C
GCCTTAAGCTCGAGCG G G
Primer
5'
GAATT CGATTTAGGTGACACTATAGAA
CTTAAGCTAAATCCACTGTGATATCTTATGT
3' arm

FIG. 16E

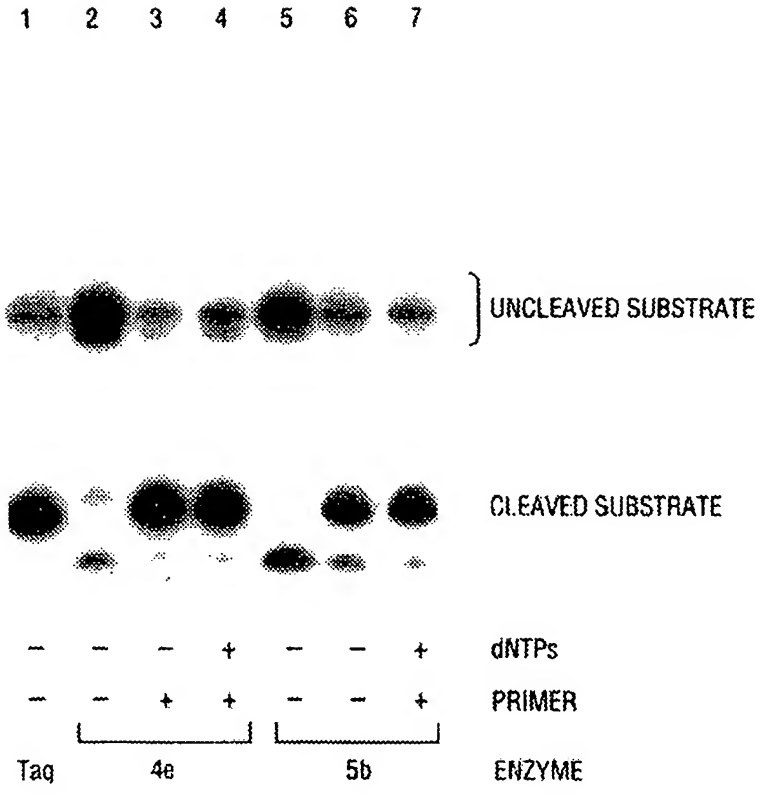

1 2 3 4 5 6 7
UNCLEAVED SUBSTRATE
CLEAVED SUBSTRATE
– – – + – – + dNTPs
– – + + – – + PRIMER
Taq 4e 5b ENZYME

FIG. 17

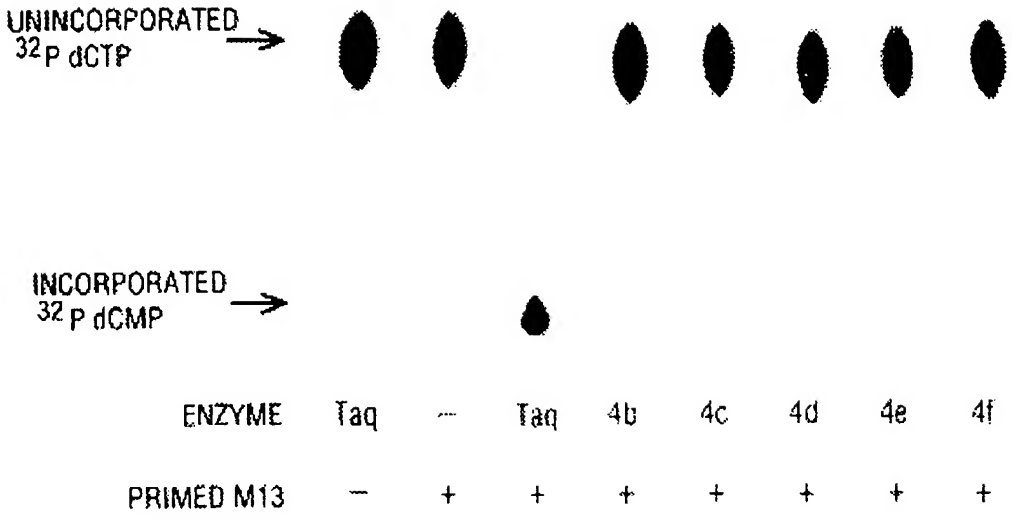

UNINCORPORATED
32 P dCTP
INCORPORATED
32 P dCMP
ENZYME Taq – Taq 4b 4c 4d 4e 4f
PRIMED M13 – + + + + + + +

FIG. 18

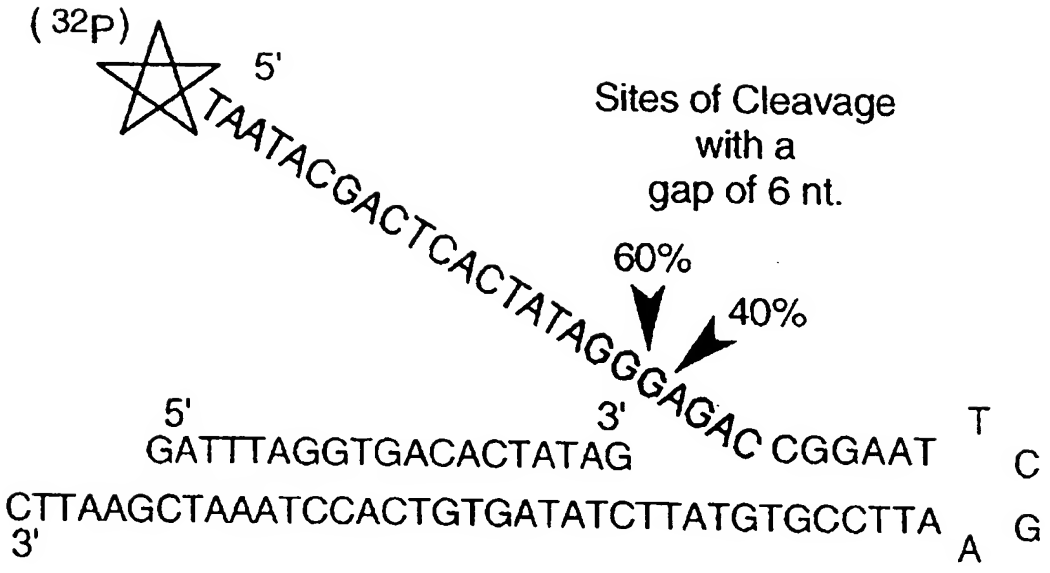

(32P)
5'
TAATACGACTCACTATAGGGAGAC
Sites of Cleavage
with a
gap of 6 nt.
60%
40%
5'
3'
GATTTAGGTGACACTATAG
CGGAAT
T
C
CTTAAGCTAAATCCACTGTGATATCTTATGTGCCTTA
A
G
3'

FIG. 19A

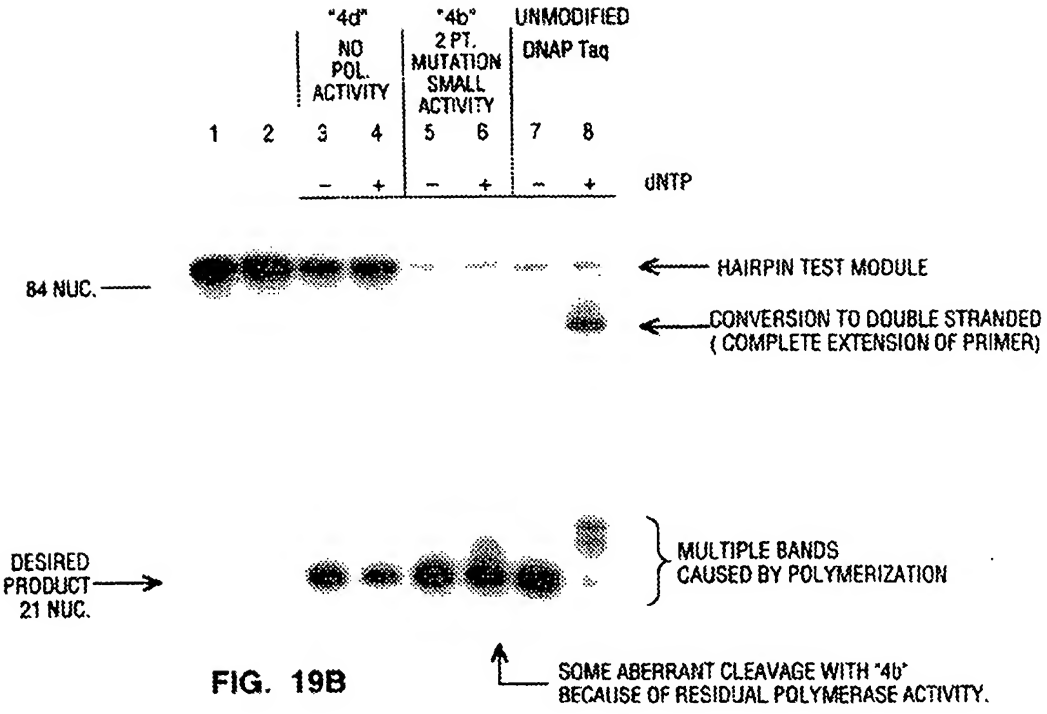

"4d"
NO POL. ACTIVITY
"4b"
2 PT. MUTATION SMALL ACTIVITY
UNMODIFIED
DNAP Taq
1 2 3 4 5 6 7 8
– + – + – +
dNTP
84 NUC.
HAIRPIN TEST MODULE
CONVERSION TO DOUBLE STRANDED
(COMPLETE EXTENSION OF PRIMER)
DESIRED PRODUCT
21 NUC.
MULTIPLE BANDS
CAUSED BY POLYMERIZATION
SOME ABERRANT CLEAVAGE WITH "4b"
BECAUSE OF RESIDUAL POLYMERASE ACTIVITY.

FIG. 19B

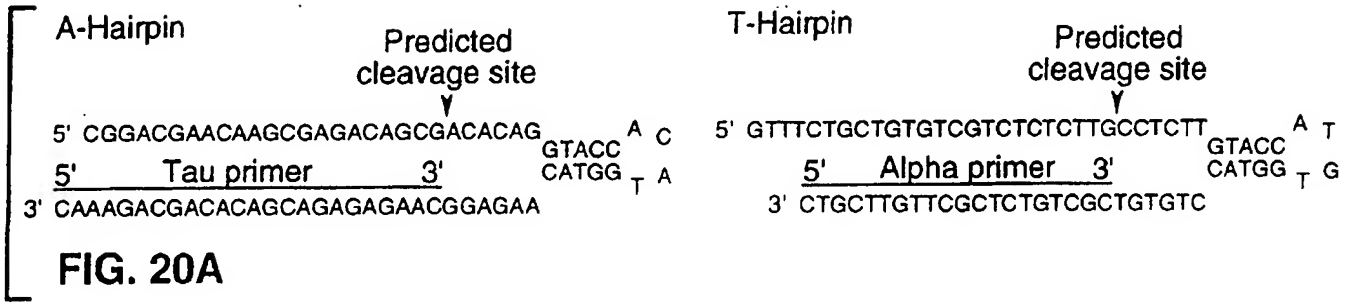


FIG. 20A

Sequence of alpha primer:
5' GACGAACAAGCGAGACAGCG 3'

FIG. 20B

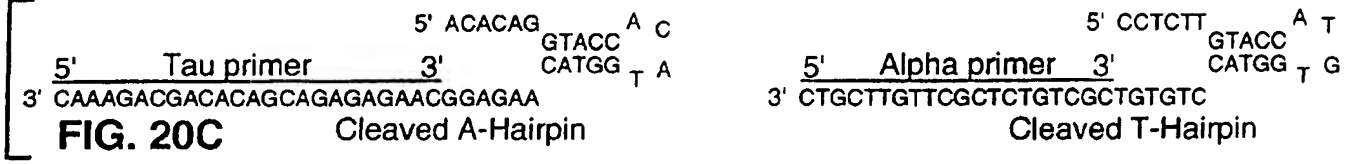


FIG. 20C

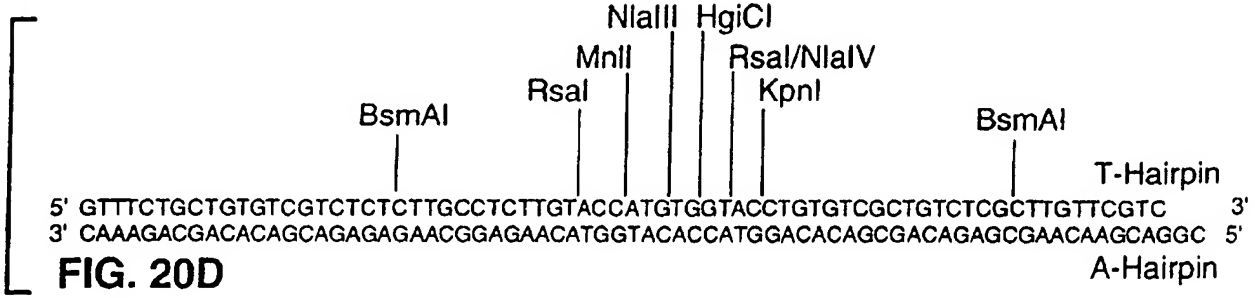


FIG. 20D

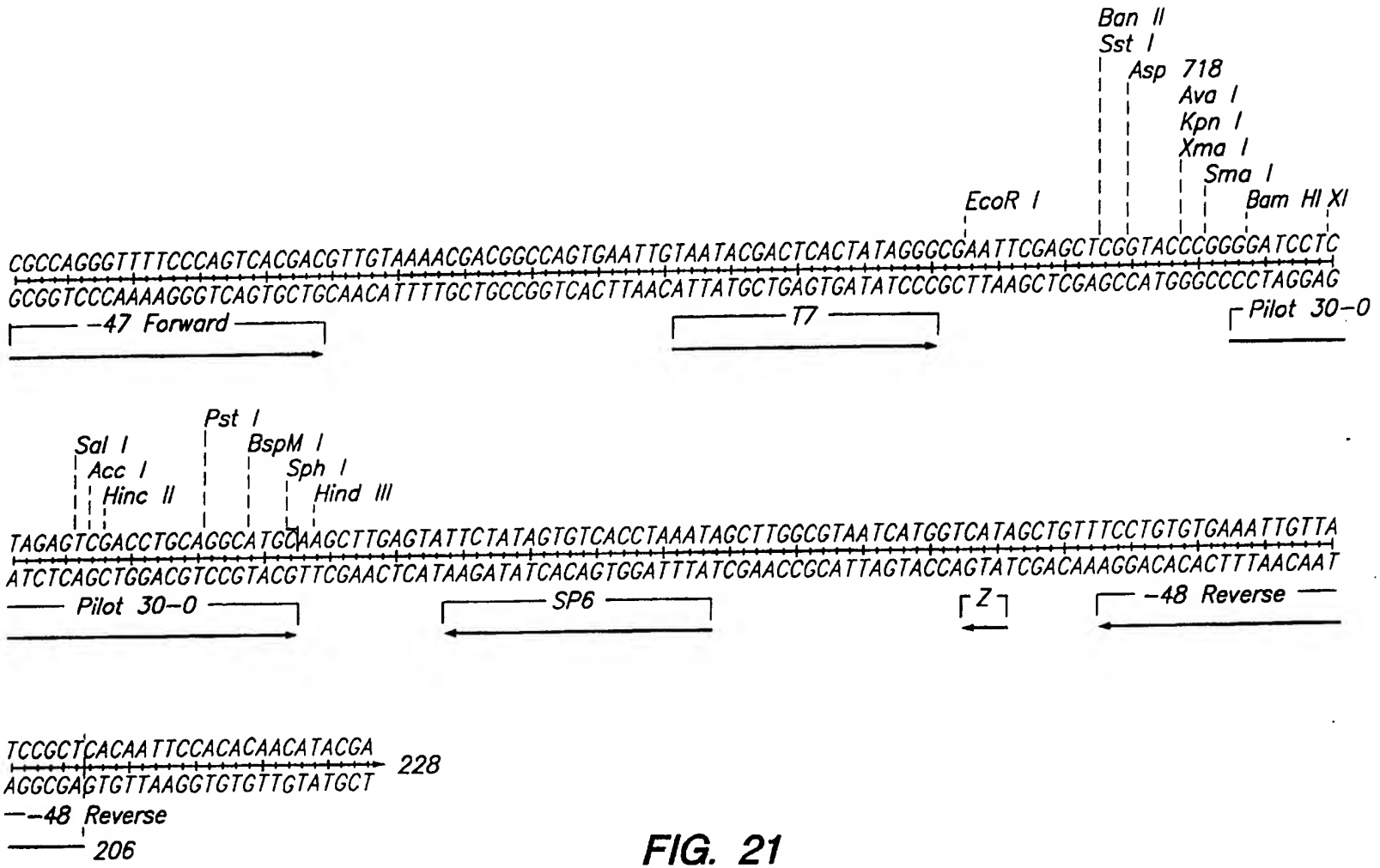

Ban II
Sst I
Asp 718
Ava I
Kpn I
Xma I
Sma I
EcoR I
Bam HI XI
CGCCAGGGTTTTCCCAGTCACGACGTTGTAAAACGACGGCCAGTGAATTGTAATACGACTCACTATAGGGCGAATTCGAGCTCGGTACCCGGGGATCCTC
GCGGTCCCAAAAGGGTCAGTGCTGCAACATTTTGCTGCCGGTCACTTAACATTATGCTGAGTGATATCCCGCTTAAGCTCGAGCCATGGGCCCCTAGGAG
-47 Forward
T7
Pilot 30-0
Pst I
Sal I
BspM I
Acc I
Sph I
Hinc II
Hind III
TAGAGTCGACCTGCAGGCATGCAAGCTTGAGTATTCTATAGTGTCACCTAAATAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTA
ATCTCAGCTGGACGTCCGTACGTTCGAACTCATAAGATATCACAGTGGATTTATCGAACCGCATTAGTACCAGTATCGACAAAGGACACACTTTAACAAT
Pilot 30-0
SP6
Z
-48 Reverse
TCCGCTCACAATTCCACACAACATACGA
228
AGGCGAGTGTTAAGGTGTGTTGTATGCT
-48 Reverse
206

FIG. 21

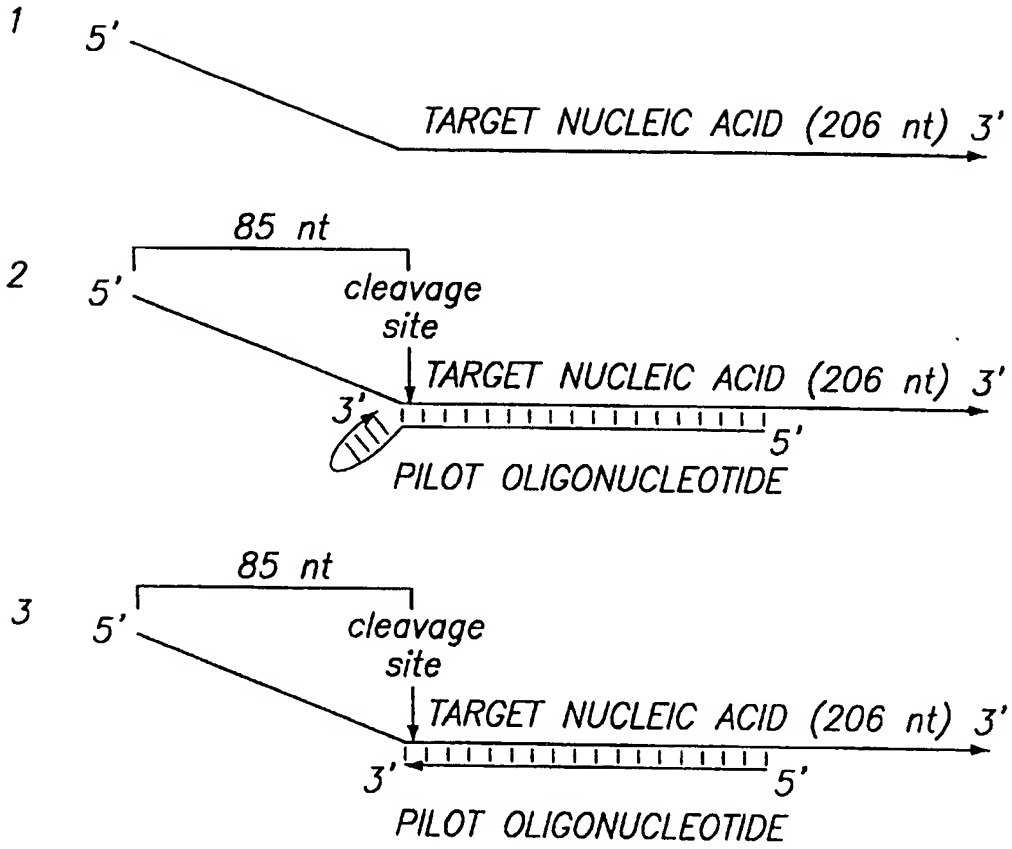

1
5'
TARGET NUCLEIC ACID (206 nt) 3'
2
85 nt
5'
cleavage site
TARGET NUCLEIC ACID (206 nt) 3'
3'
5'
PILOT OLIGONUCLEOTIDE
3
85 nt
5'
cleavage site
TARGET NUCLEIC ACID (206 nt) 3'
3'
5'
PILOT OLIGONUCLEOTIDE

FIG. 22A

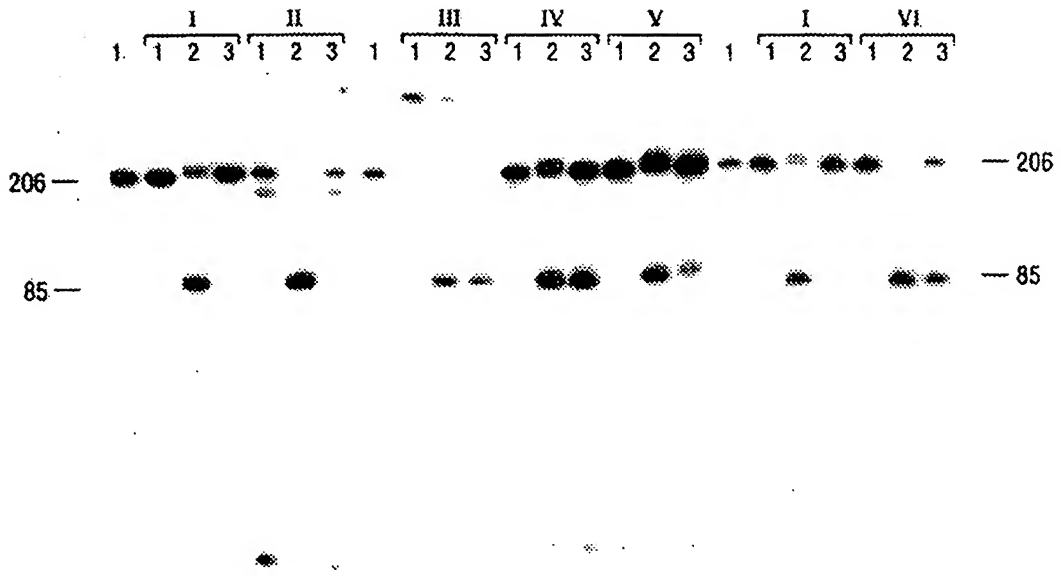


FIG. 22B

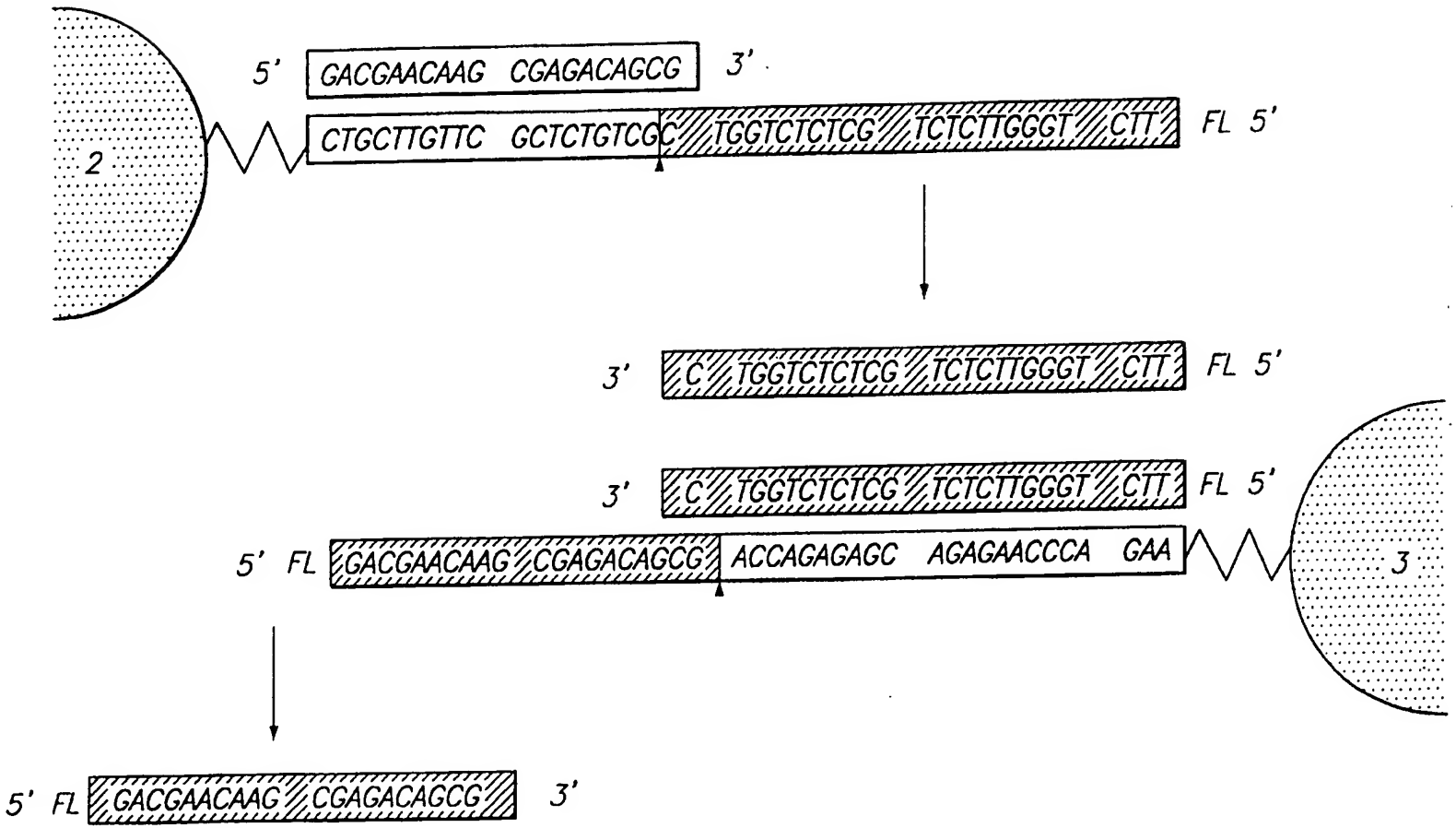

5'
GACGAACAAG CGAGACAGCG
3'
2
CTGCTTGTTC GCTCTGTCGC TGGTCTCTCG TCTCTTGGGT CTT
FL 5'
3'
C TGGTCTCTCG TCTCTTGGGT CTT
FL 5'
3'
C TGGTCTCTCG TCTCTTGGGT CTT
FL 5'
5' FL
GACGAACAAG CGAGACAGCG
ACCAGAGAGC AGAGAACCCA GAA
3
5' FL
GACGAACAAG CGAGACAGCG
3'

FIG. 23

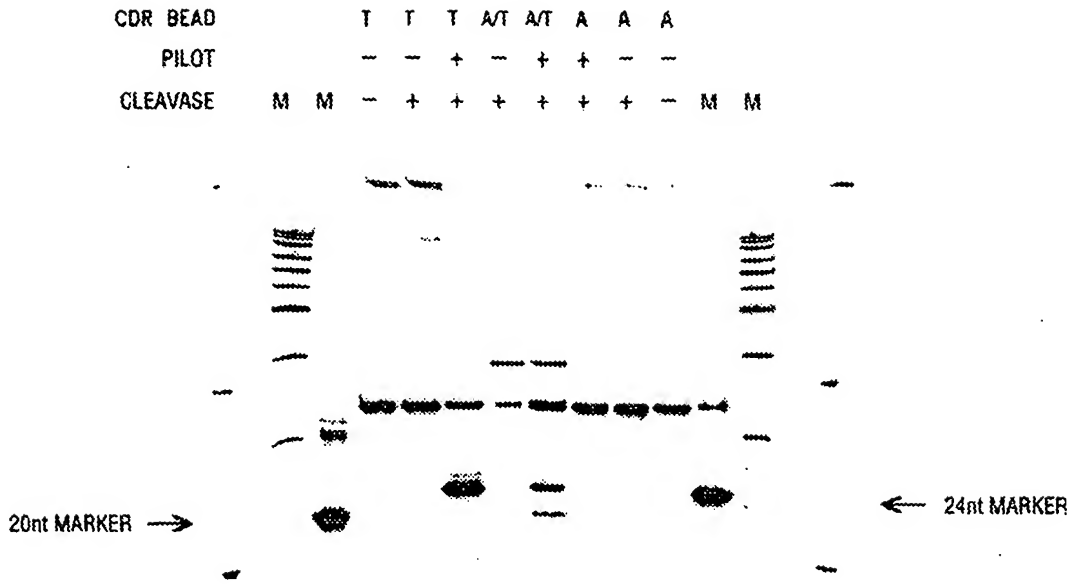

CDR BEAD
PILOT
CLEAVASE
T T T A/T A/T A A A
M M − + + + + + + − M M
20nt MARKER
24nt MARKER

FIG. 24

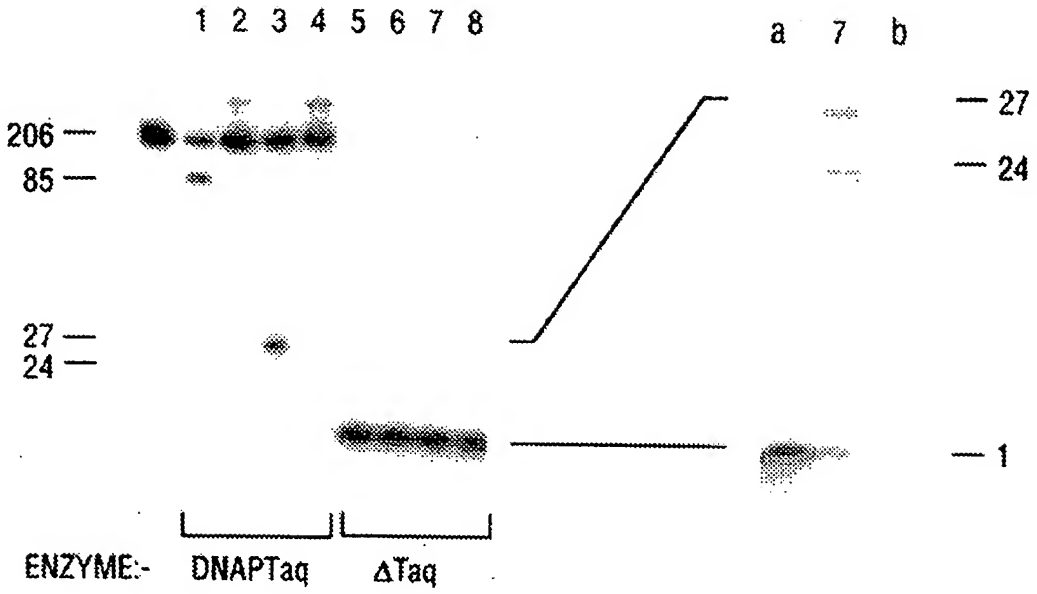


FIG. 25A

FIG. 25B

FIG. 26A

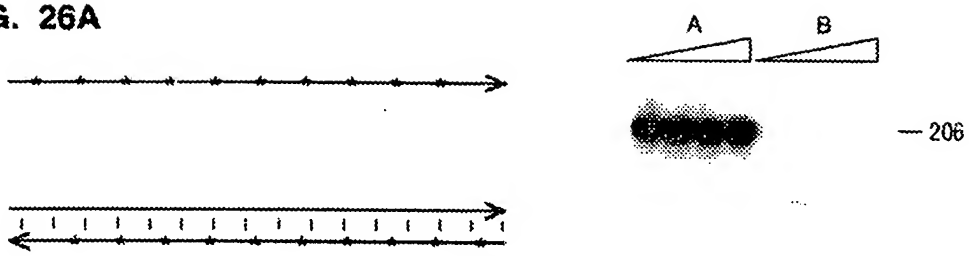


FIG. 26B

* = ^{32}P

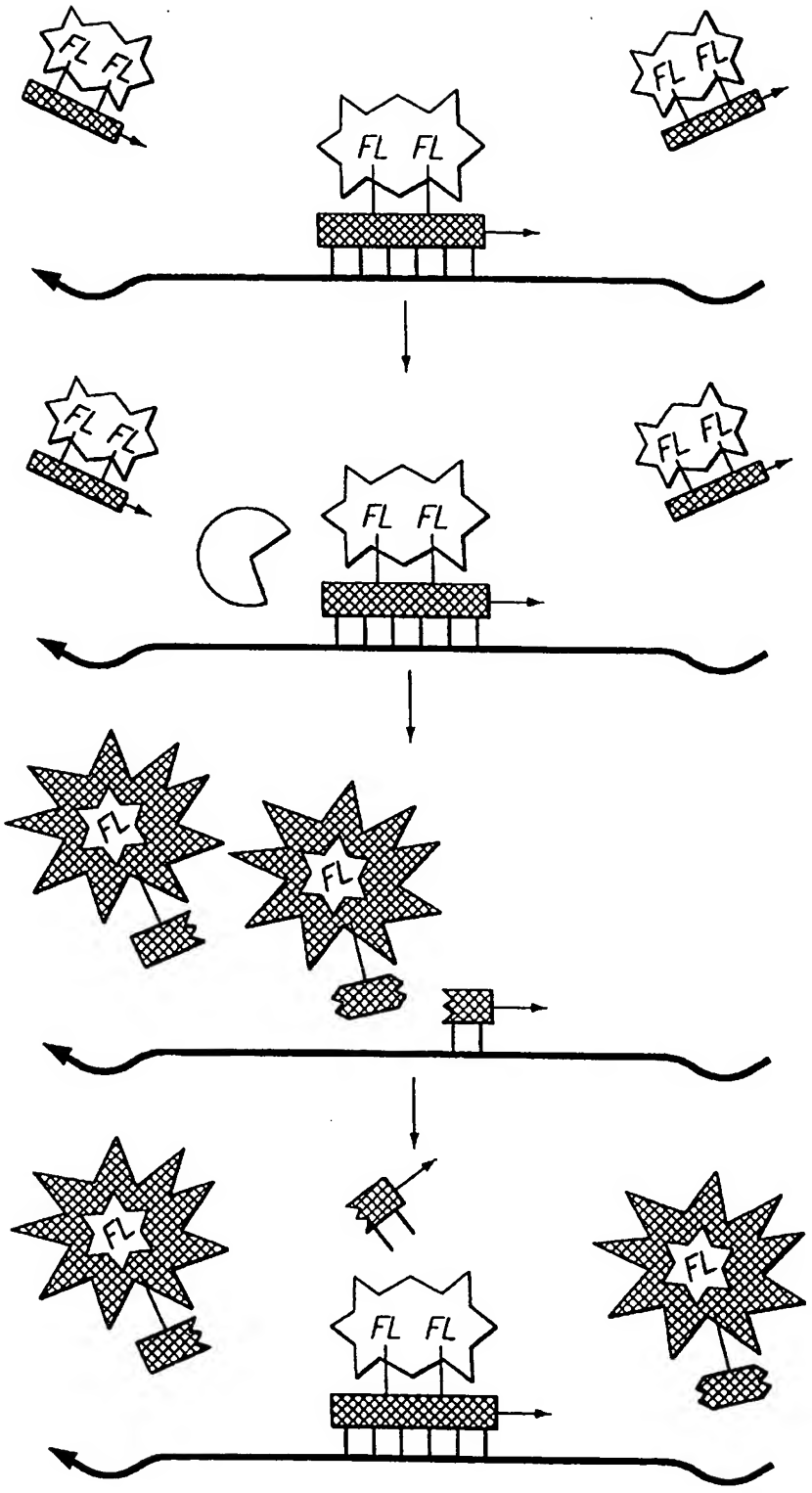


FIG. 27

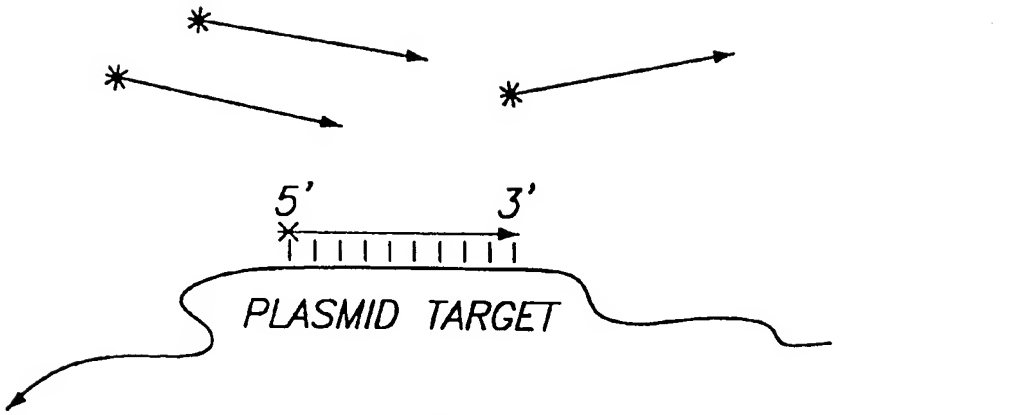


FIG. 28A

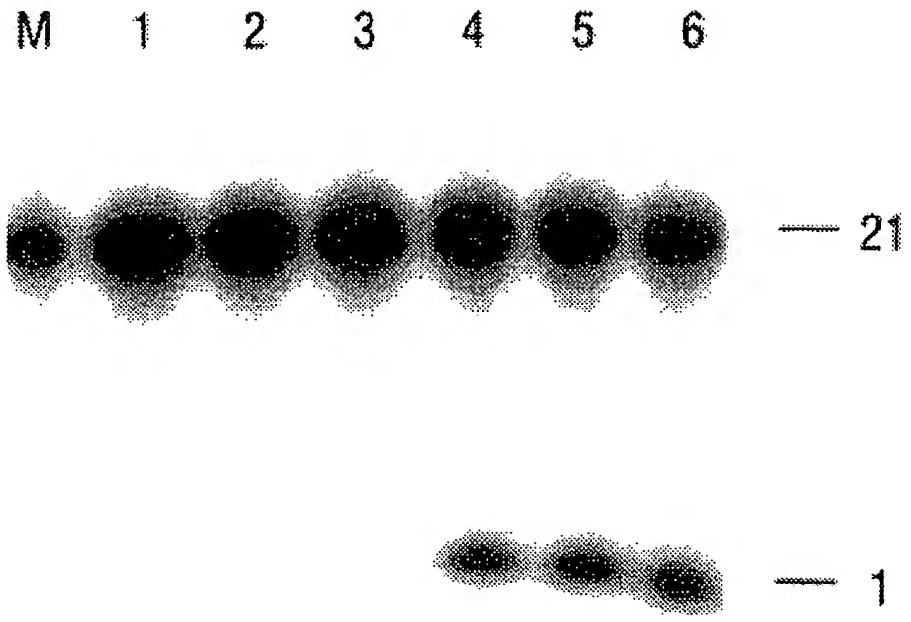


FIG. 28B

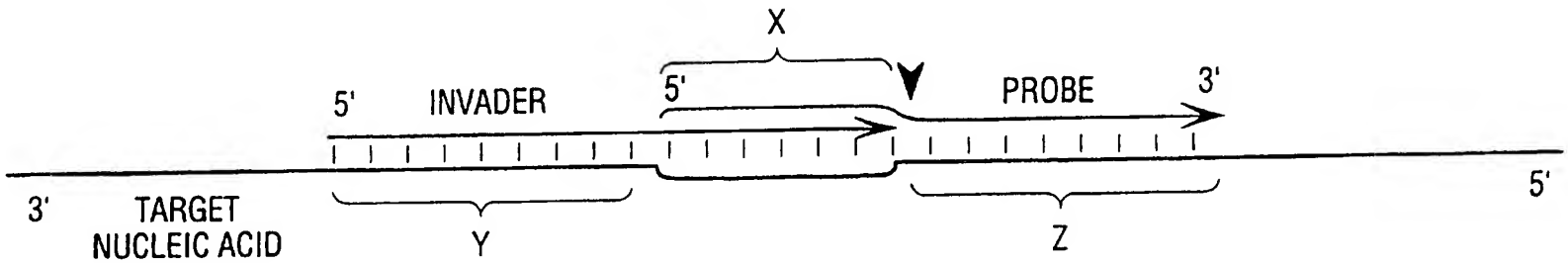


FIG. 29

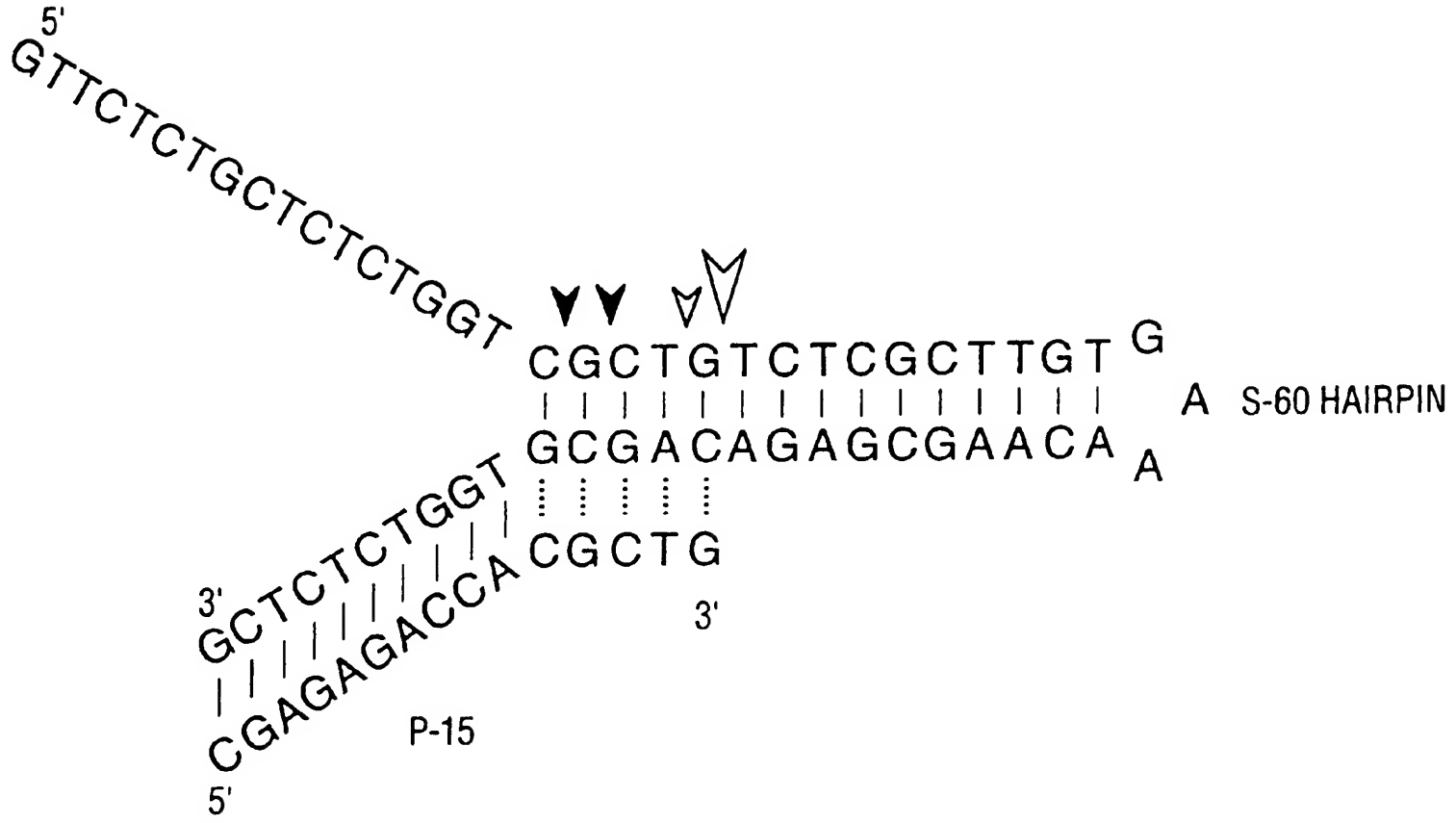

5'
GTTCTCTGCTCTCTGGT
CGCTGTCTCGCTTGT G
A
S-60 HAIRPIN
GCGACAGAGCGAACA A
GCTCTCTGGT
CGCTG
3'
3'
GCTCTCTGGT
CGAGAGACCA
P-15
5'

FIG. 30

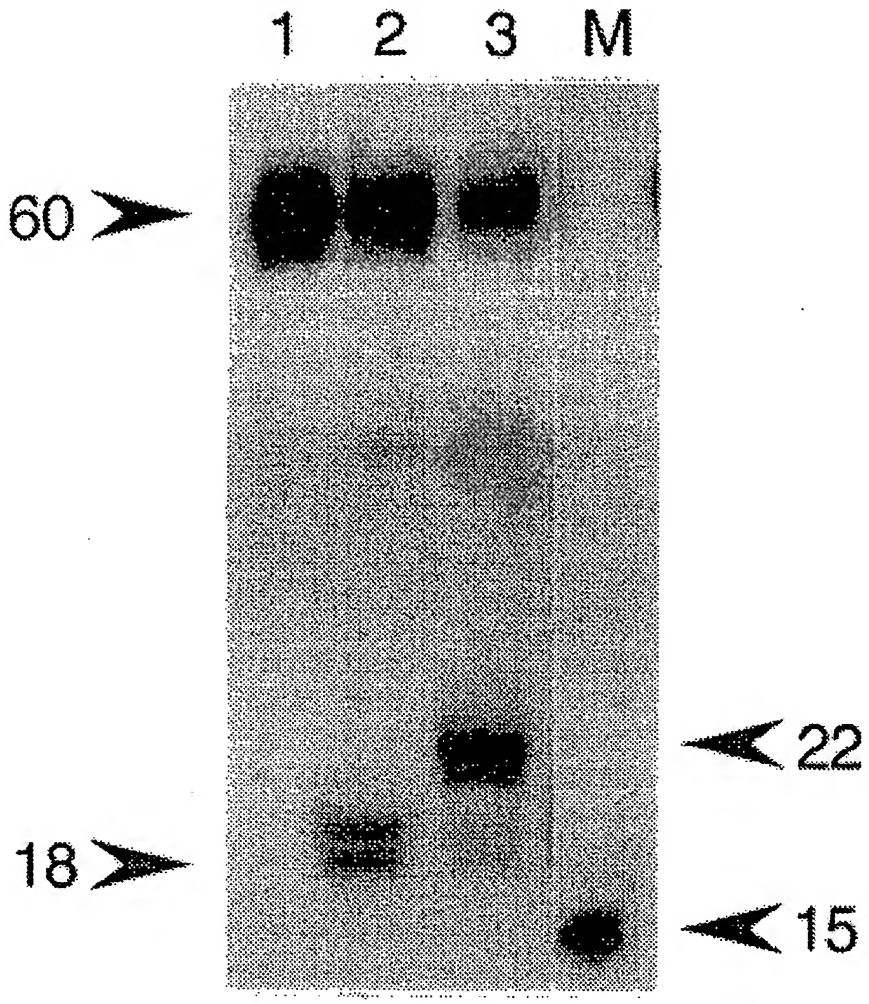


FIG. 31

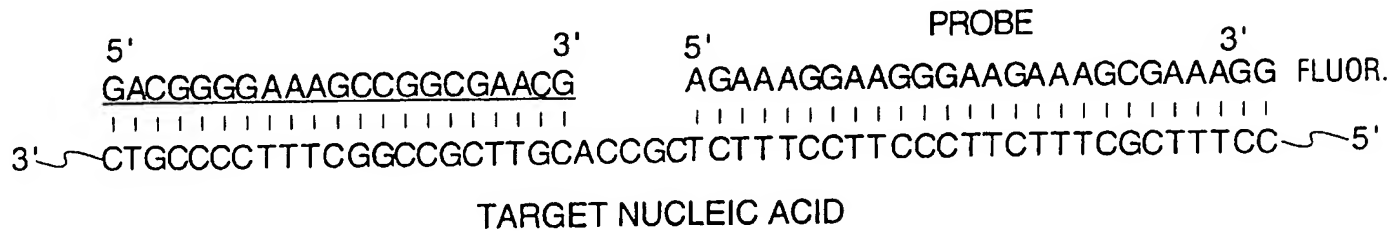


FIG. 32A

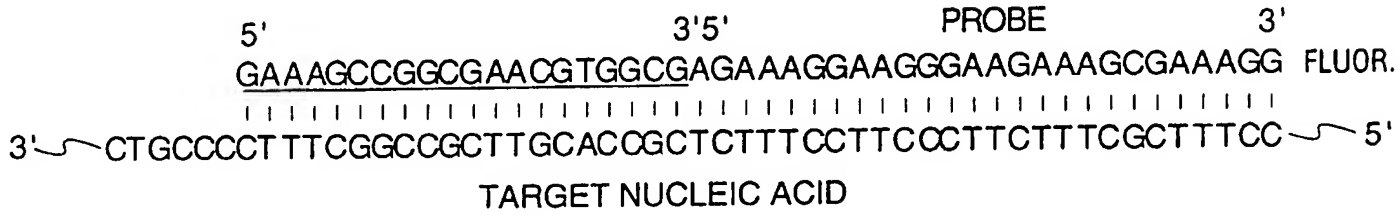


FIG. 32B

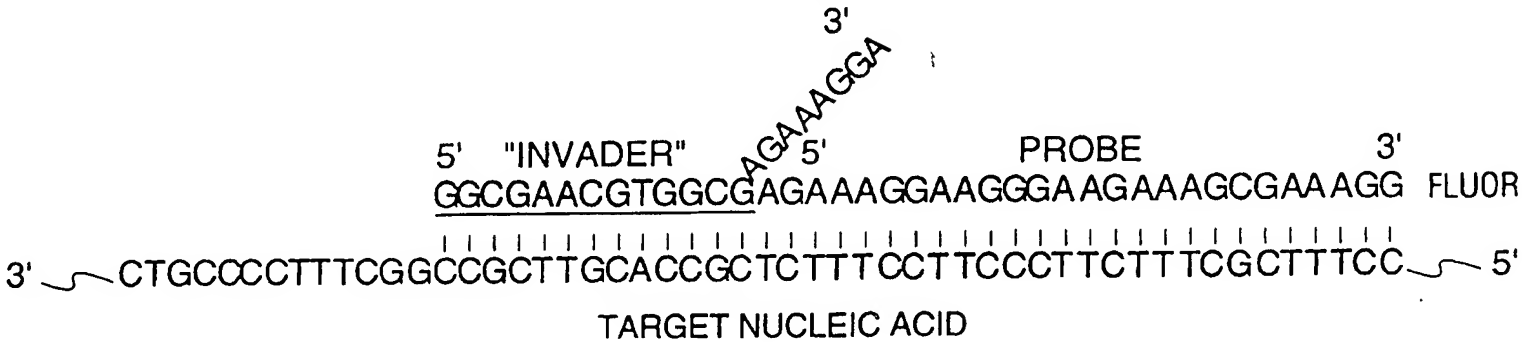


FIG. 32C

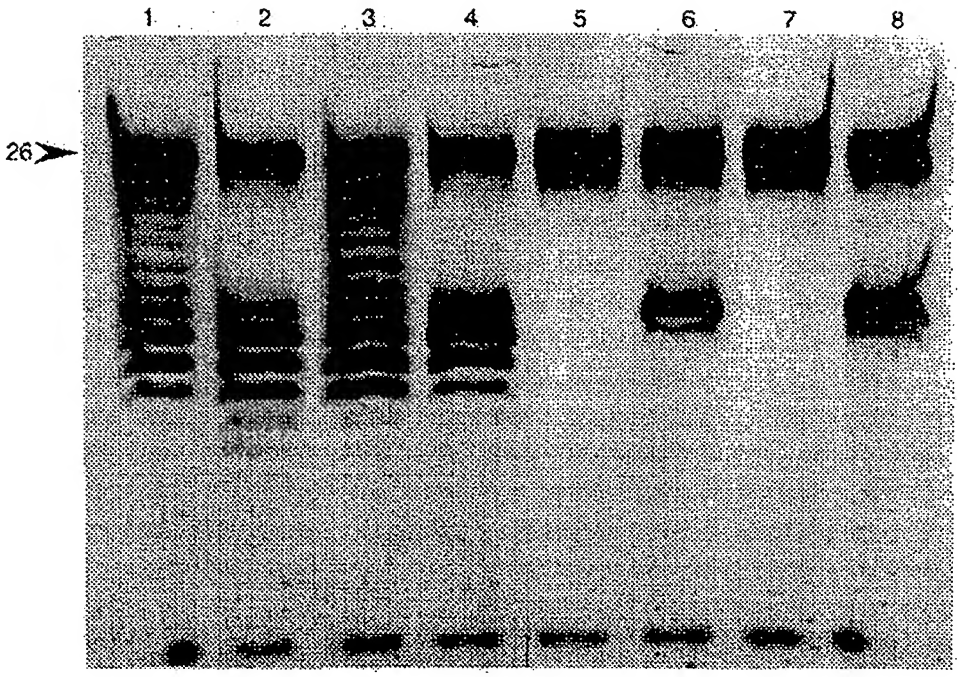


FIG. 33

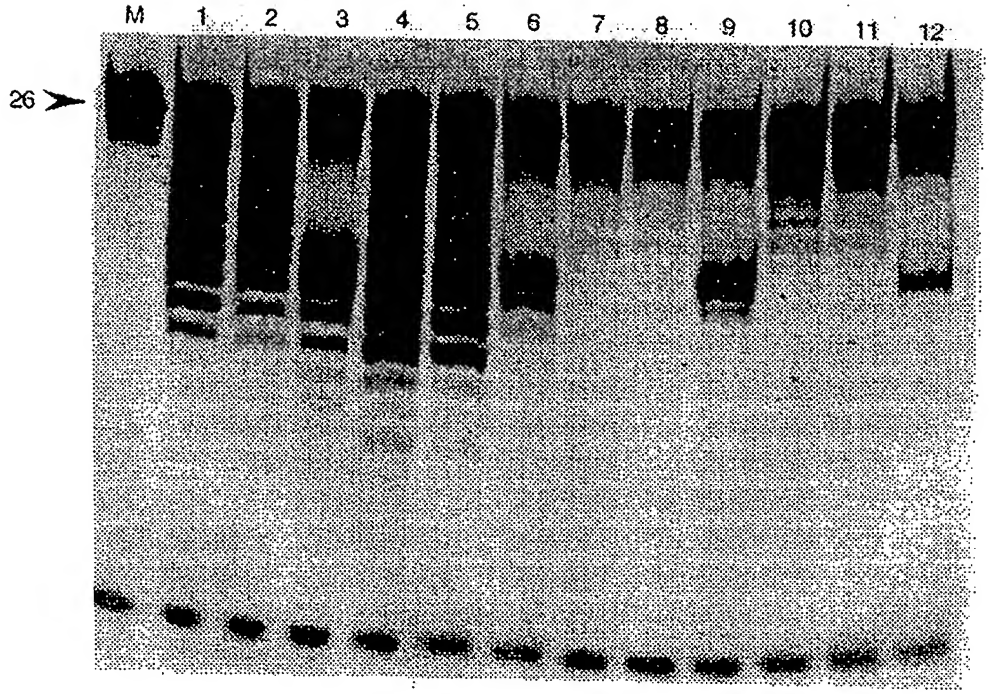


FIG. 34

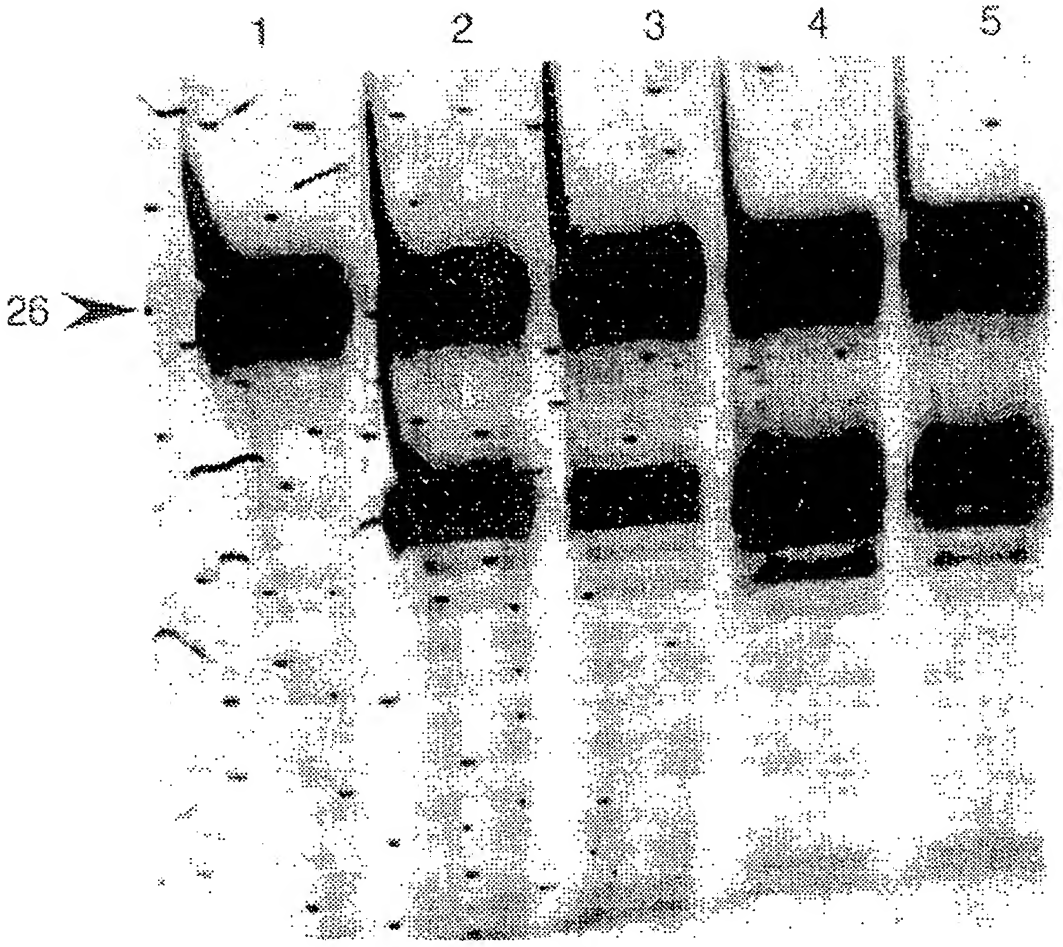


FIG. 35

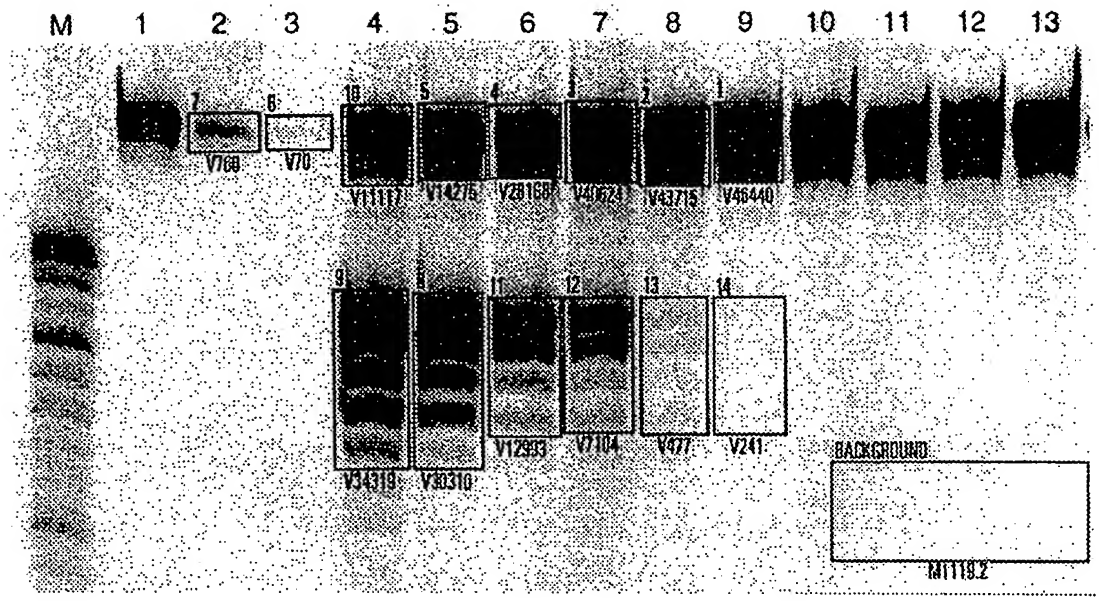

M
1
2
3
4
5
6
7
8
9
10
11
12
13
V768
V70
V11117
V14276
V28168
V40624
V43715
V46440
V34319
V38310
V12993
V7104
V477
V241
BACKGROUND
MI119.2

FIG. 36

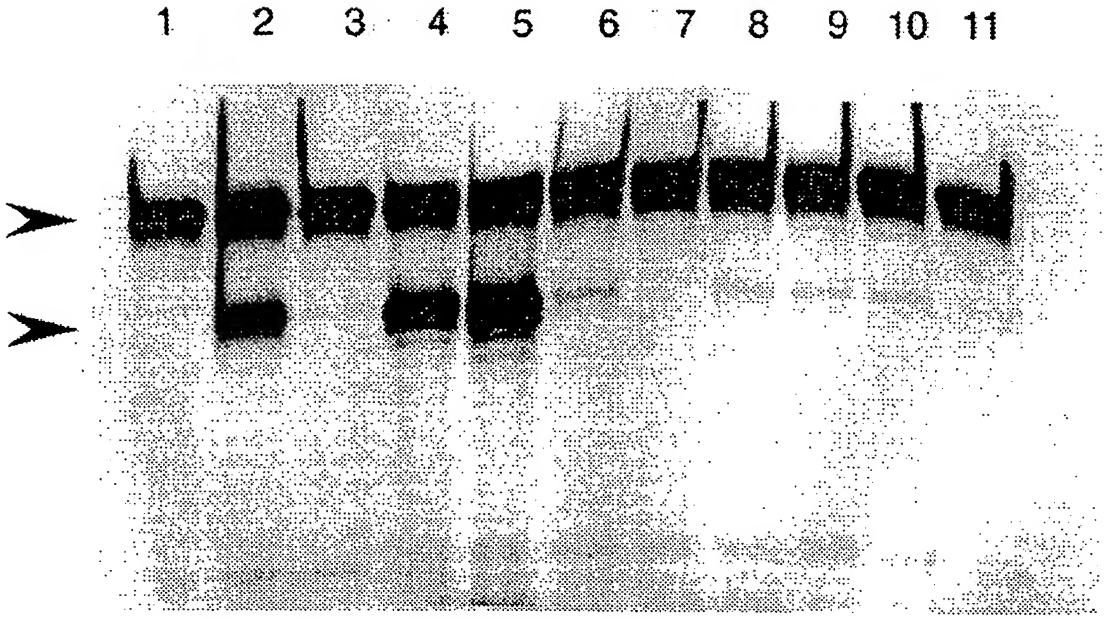


FIG. 37

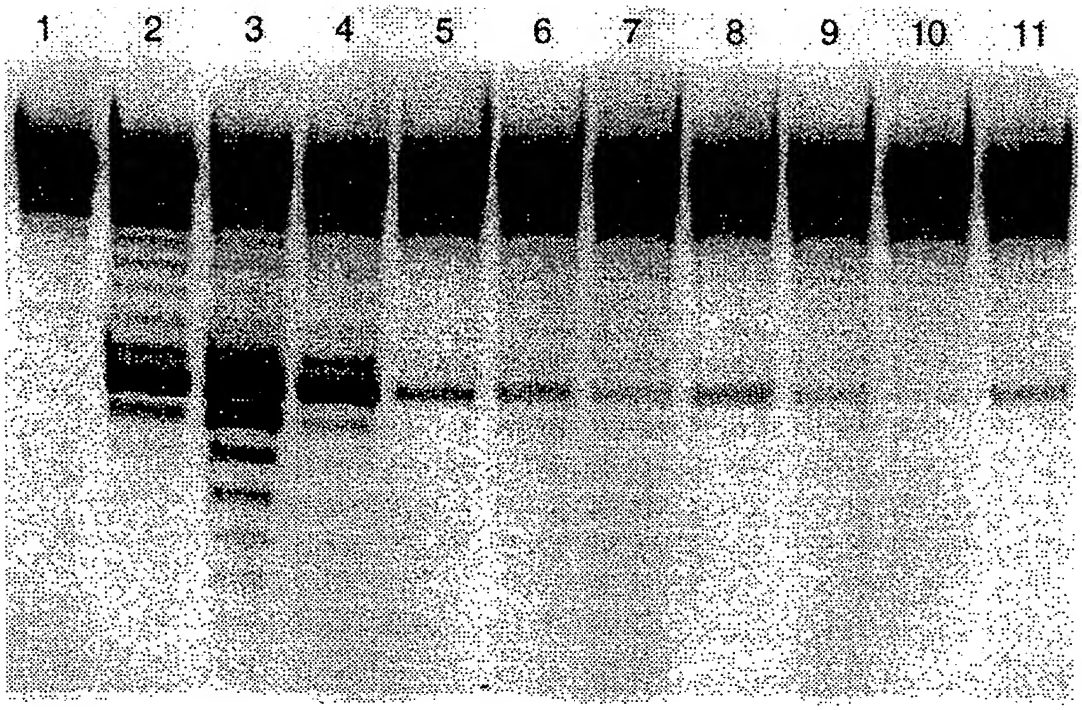


FIG. 38

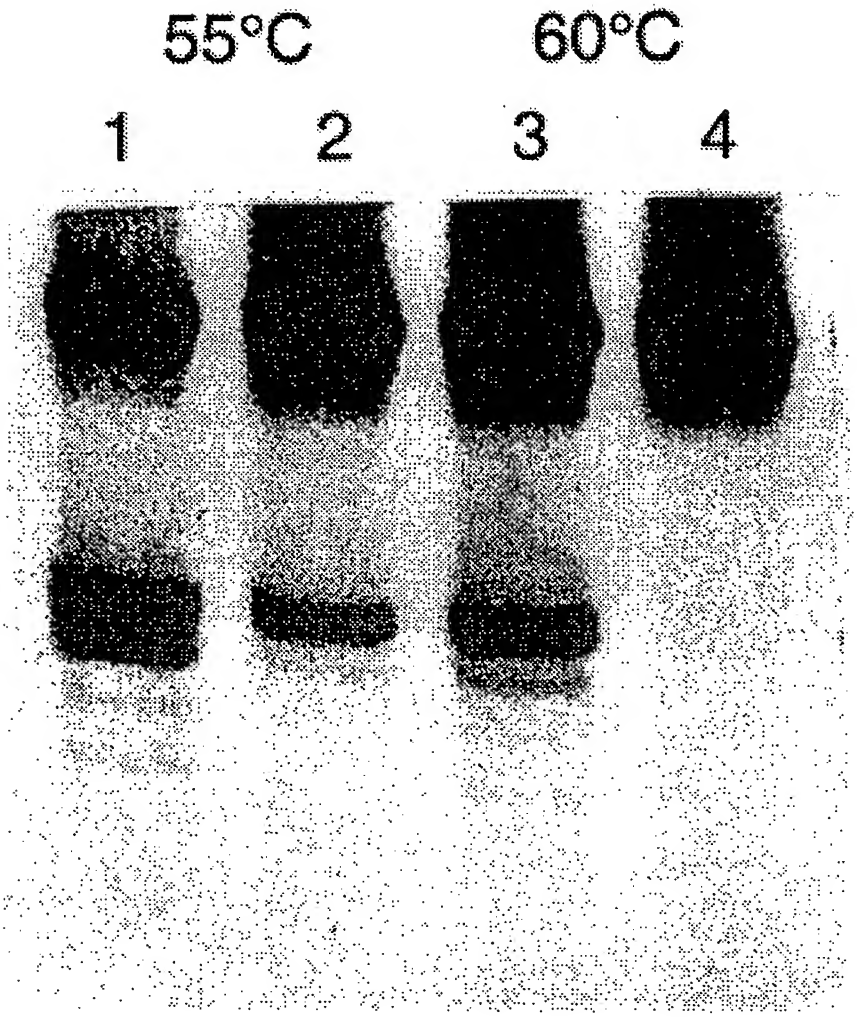


FIG. 39

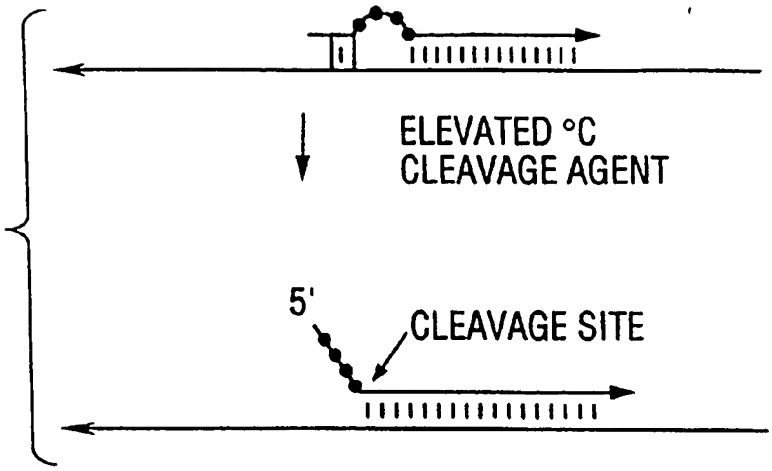


FIG. 40A

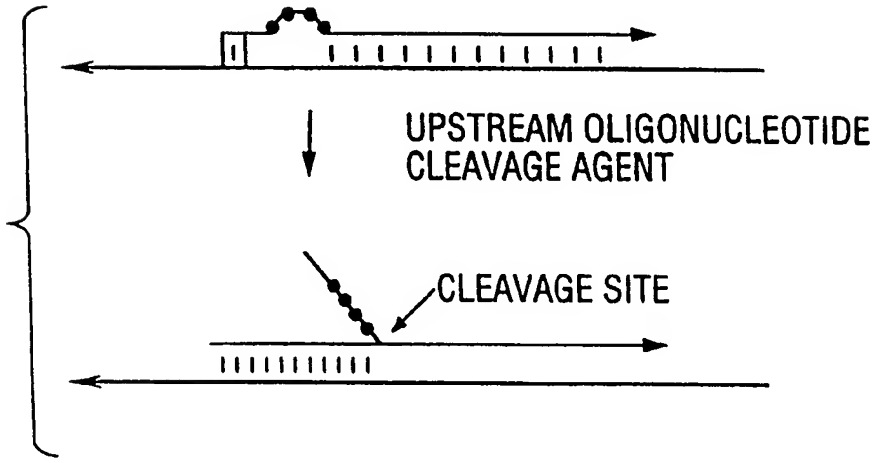


FIG. 40B

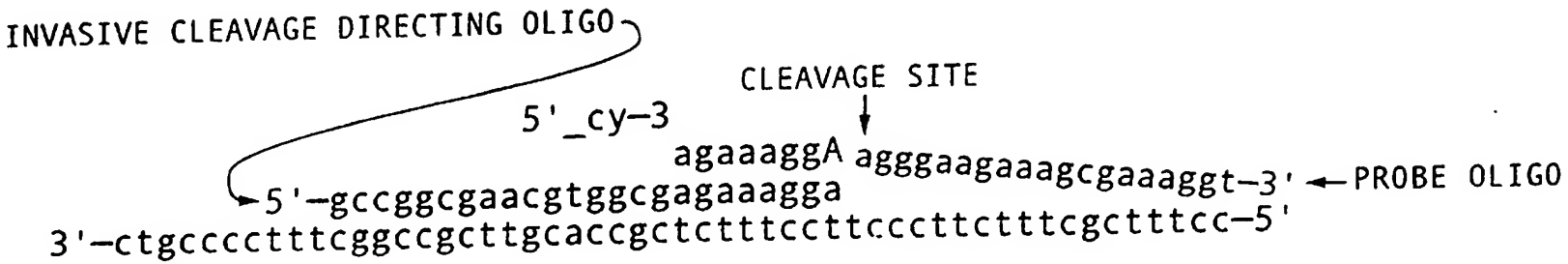

INVASIVE CLEAVAGE DIRECTING OLIGO
CLEAVAGE SITE
5'_cy–3
agaaaggA agggaagaaagcgaaaggt–3'
PROBE OLIGO
5'–gccggcgaacgtggcgagaaagga
3'–ctgccccttcggccgcttgcaccgctctttccttcccttctttcgctttcc–5'

FIG. 41

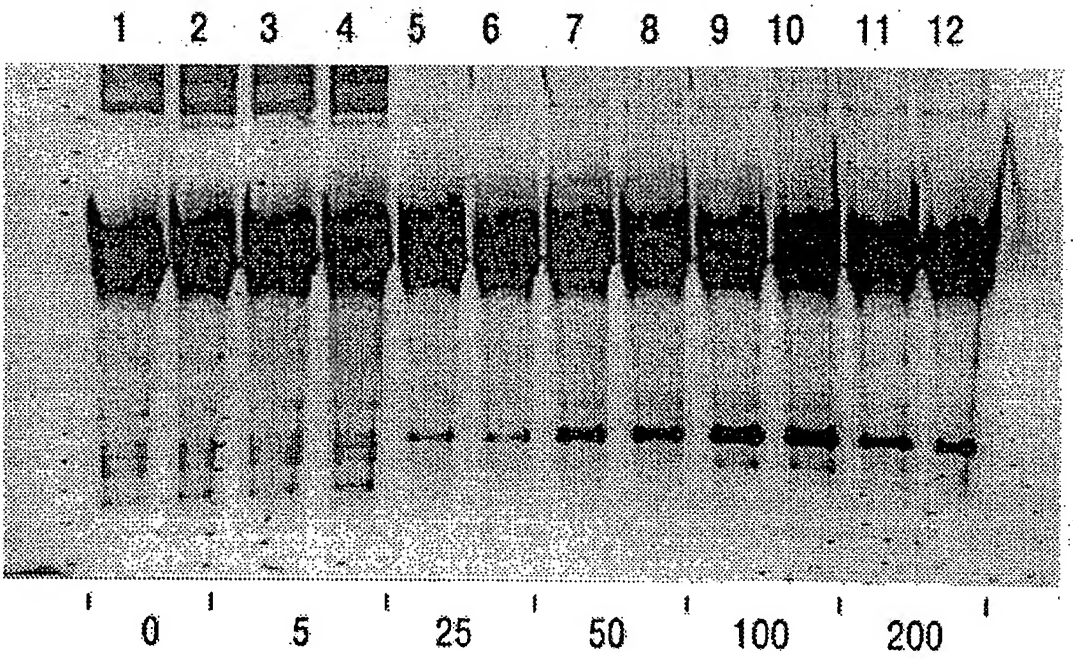


FIG. 42

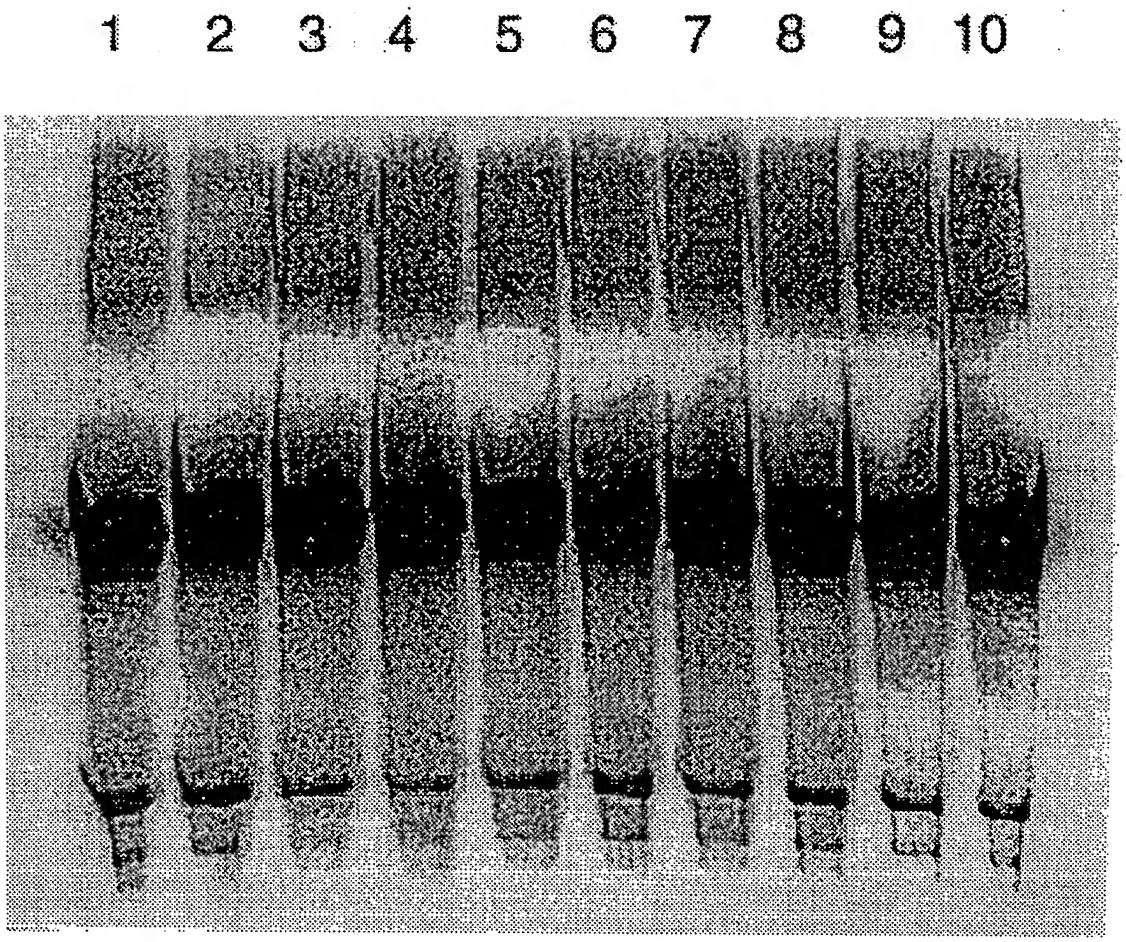


FIG. 43

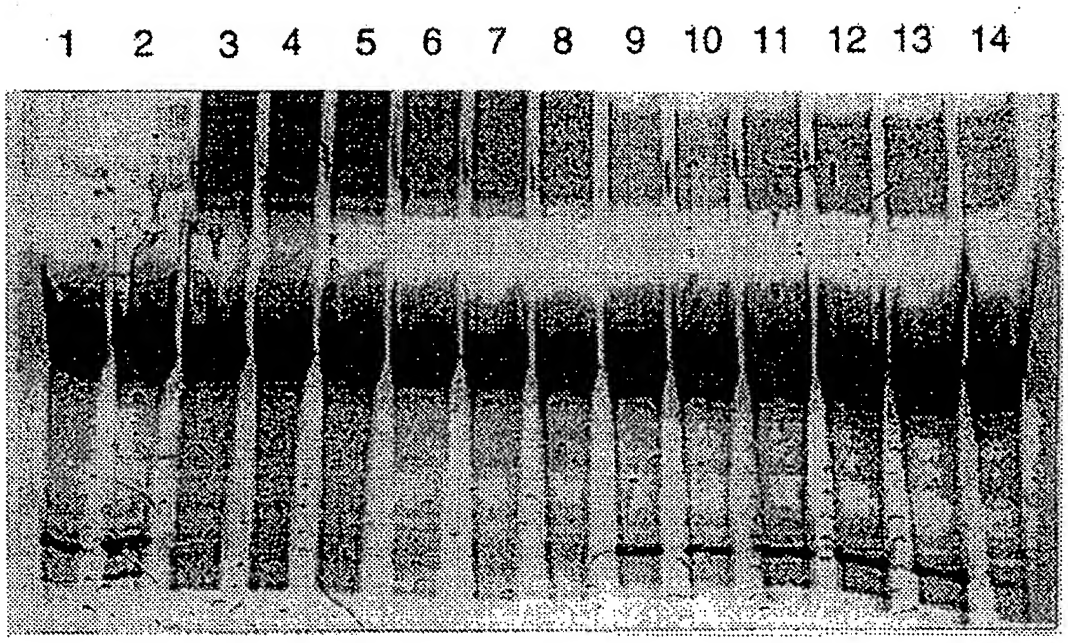


FIG. 44

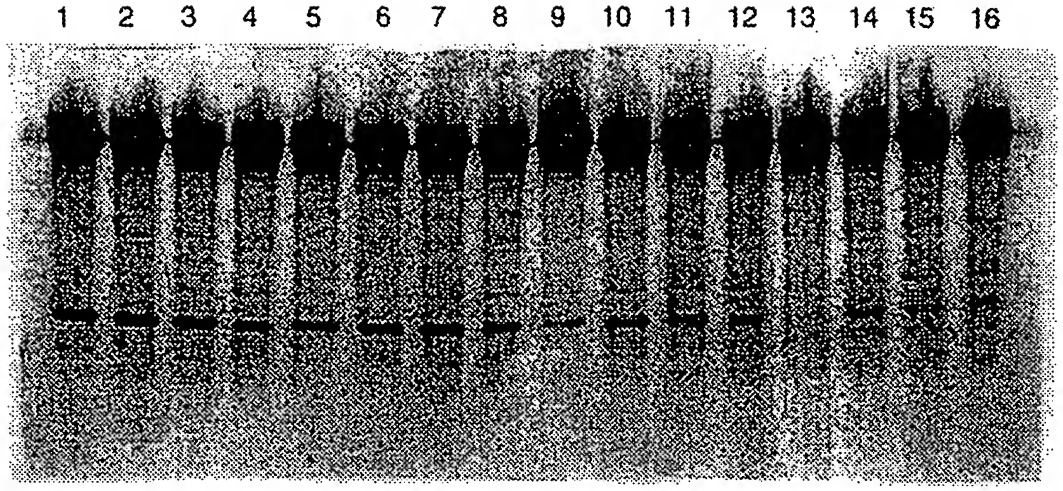


FIG. 45

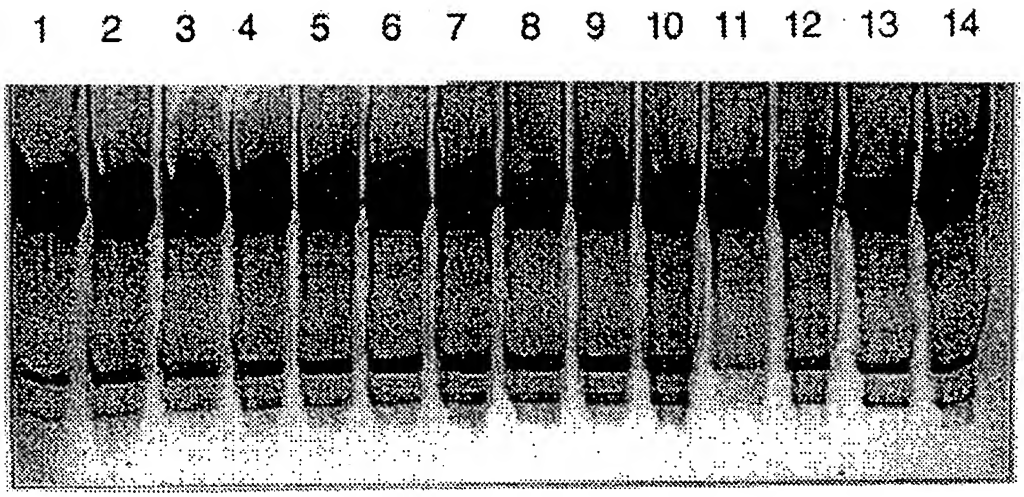


FIG. 46

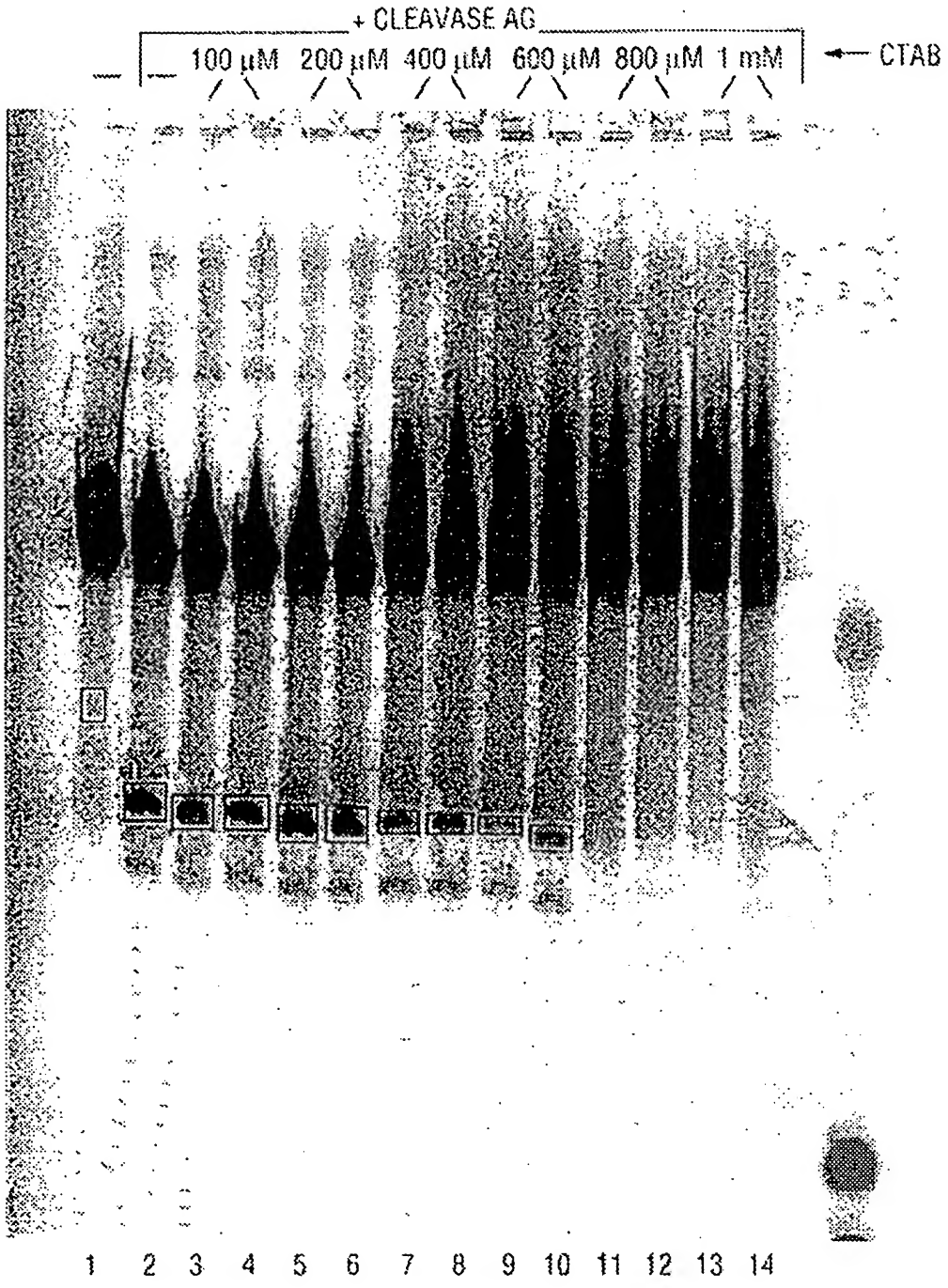

+ CLEAVASE AG
100 µM 200 µM 400 µM 600 µM 800 µM 1 mM
CTAB
1 2 3 4 5 6 7 8 9 10 11 12 13 14

FIG. 47

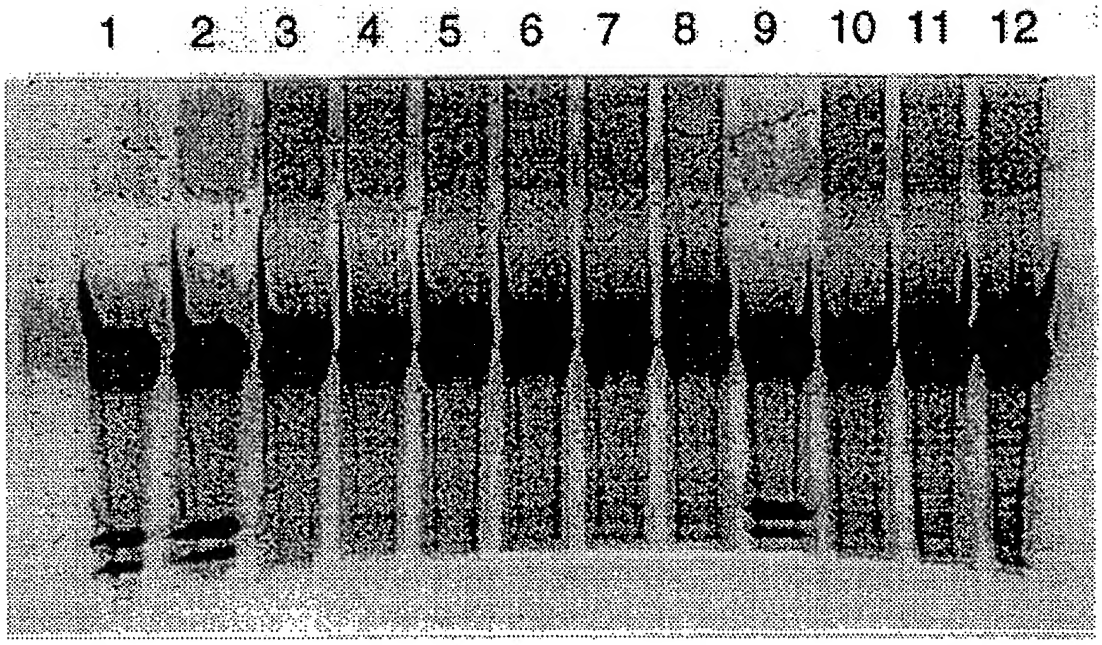


FIG. 48

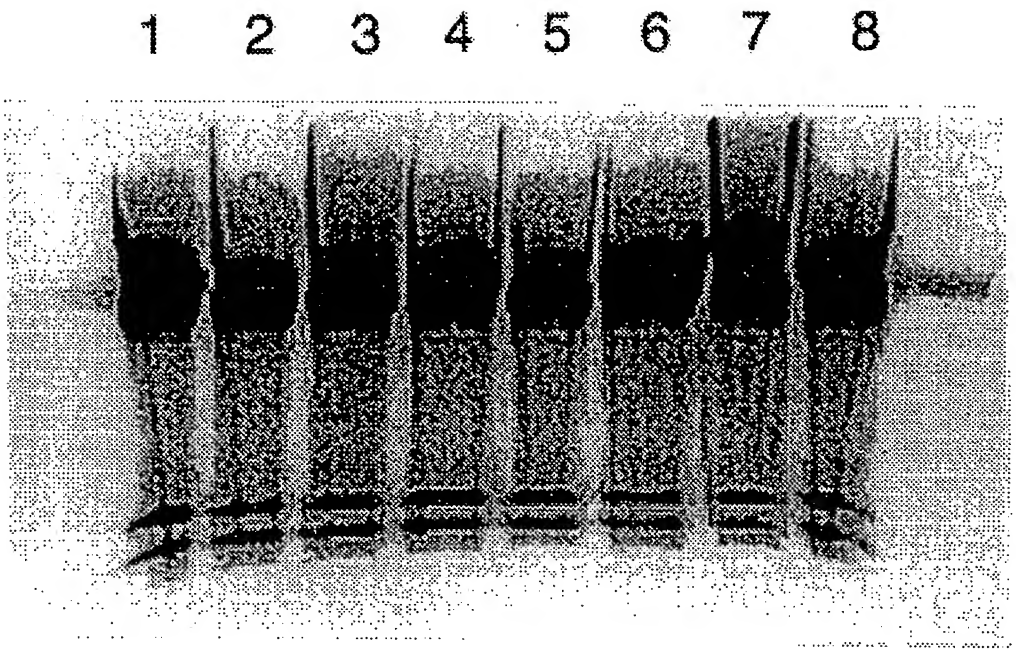


FIG. 49

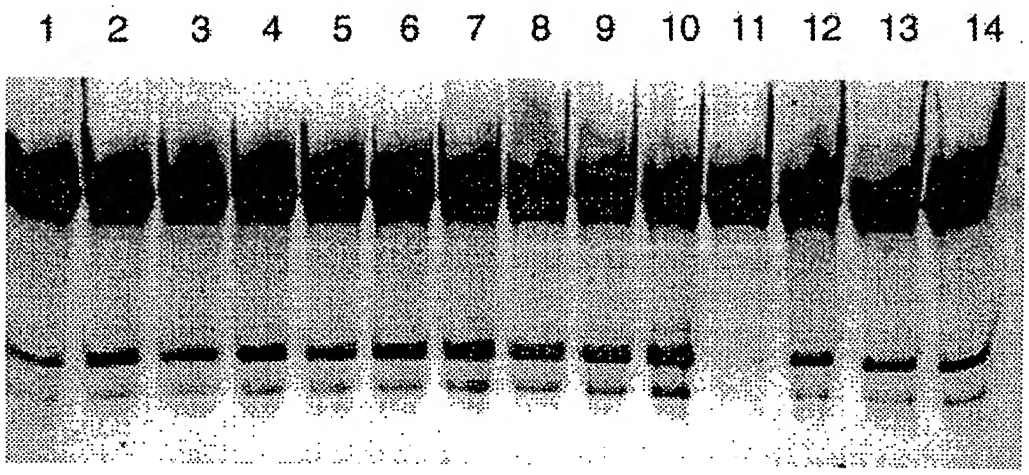


FIG. 50

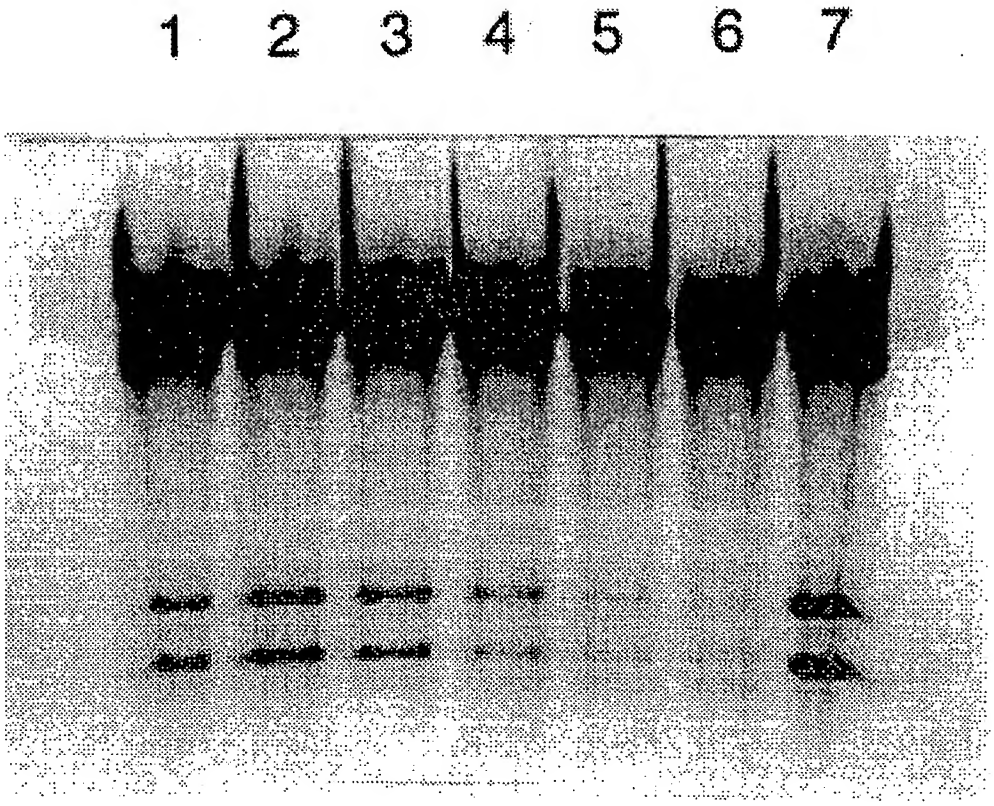


FIG. 51

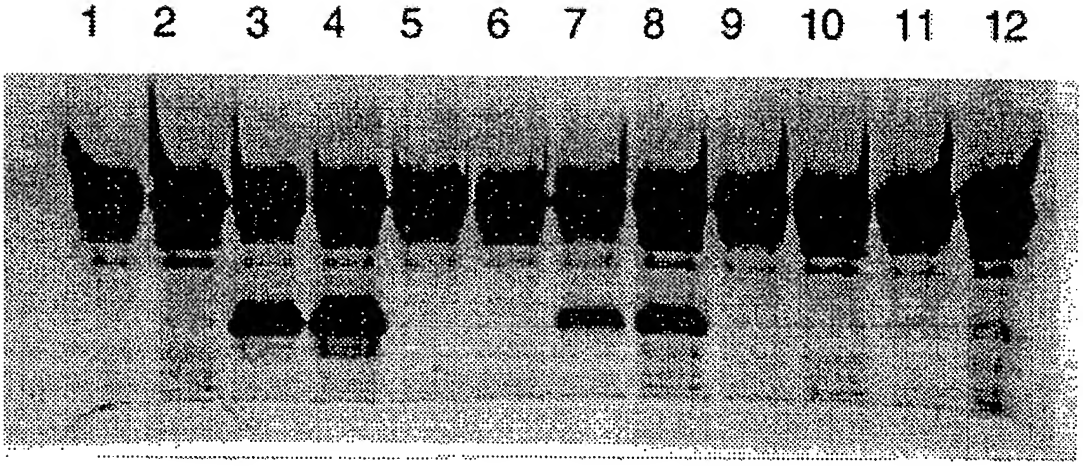


FIG. 52

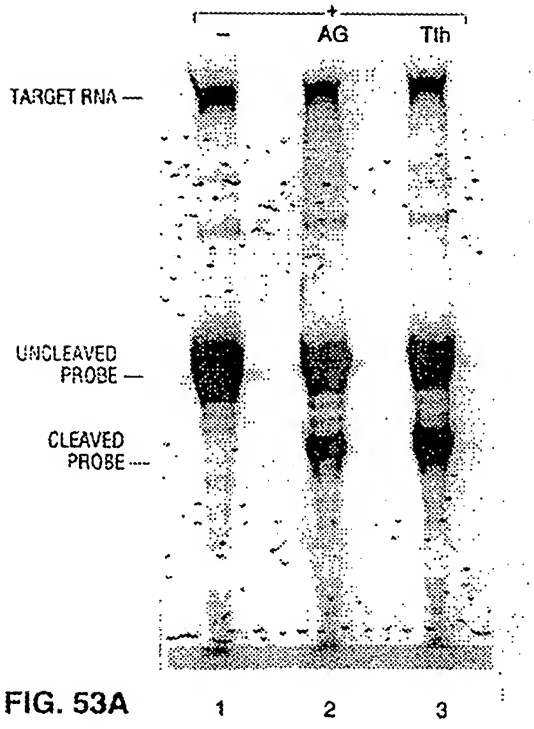


FIG. 53A

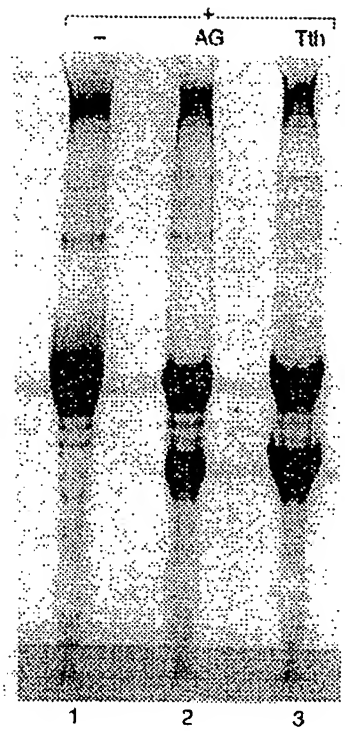


FIG. 53B

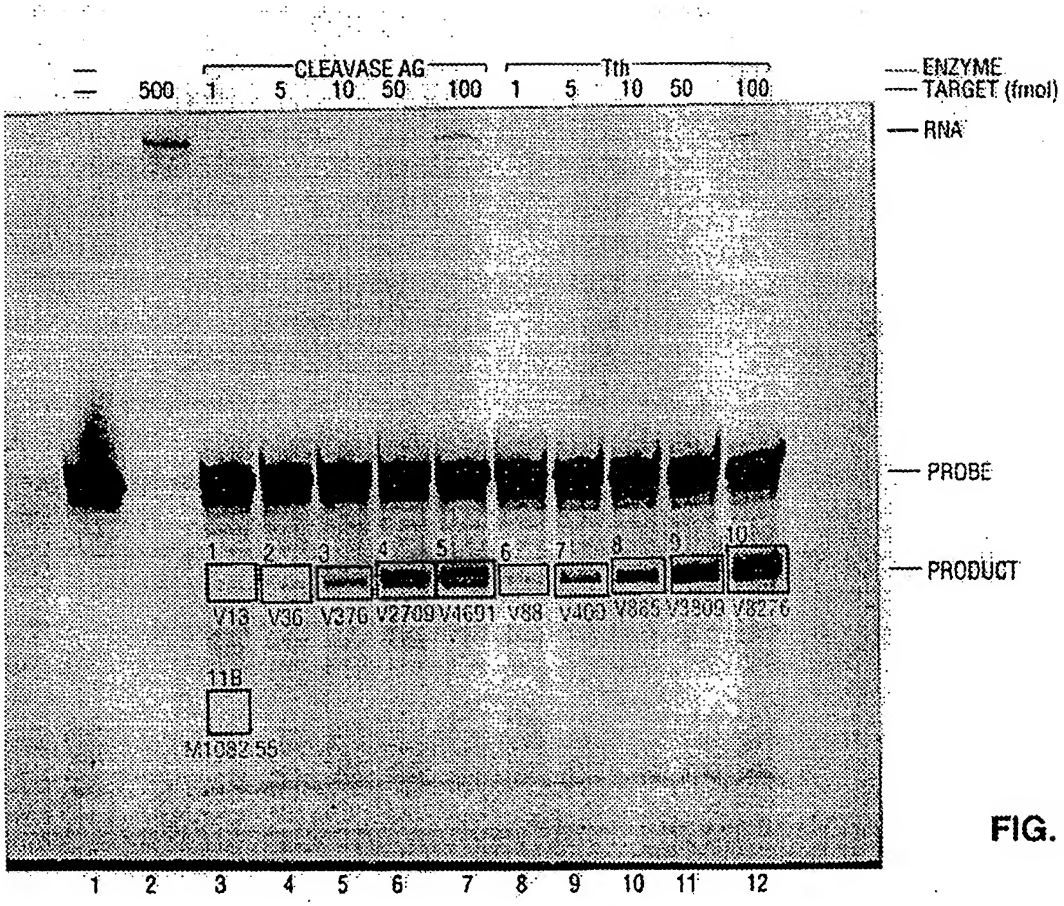

CLEAVASE AG
Tth
ENZYME
TARGET (fmol)
500
1
5
10
50
100
1
5
10
50
100
RNA
PROBE
PRODUCT
1
2
3
4
5
6
7
8
9
10
V13
V36
V376
V2709
V4601
V88
V400
V385
V2309
V8276
11B
M1082-55
1
2
3
4
5
6
7
8
9
10
11
12

FIG. 54

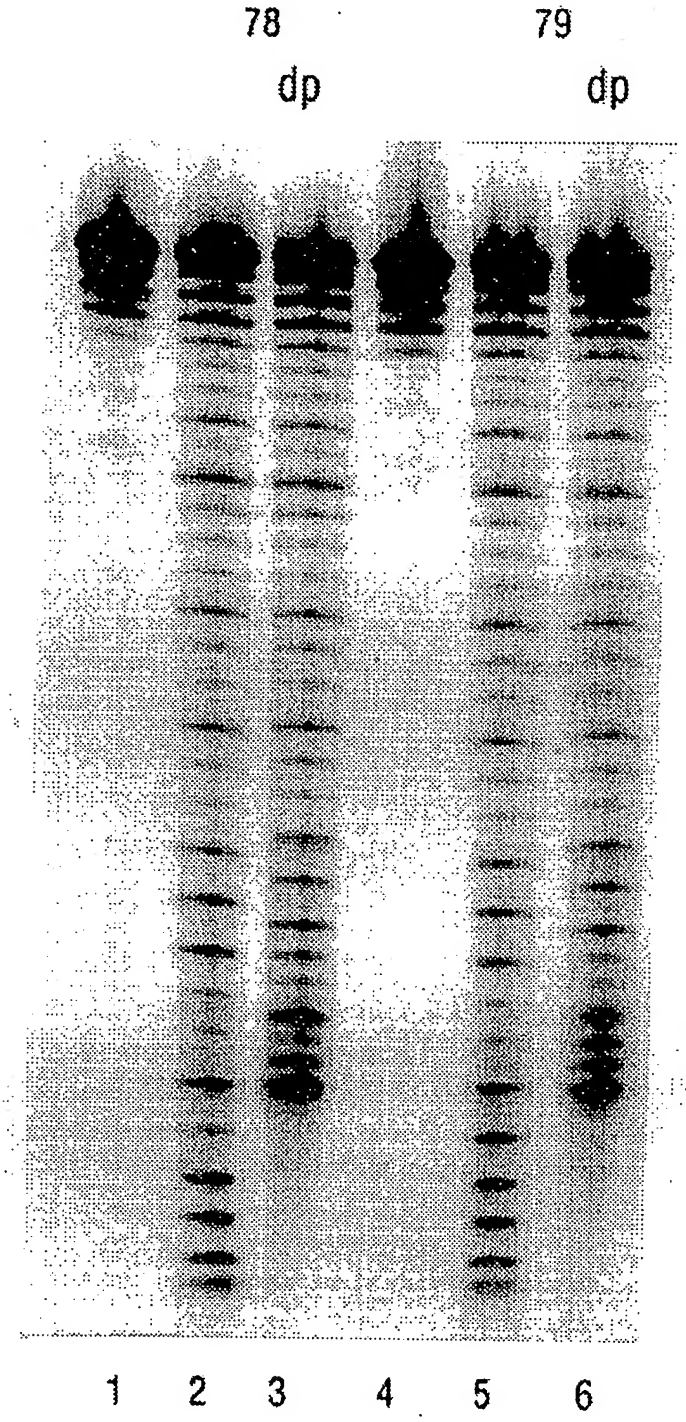
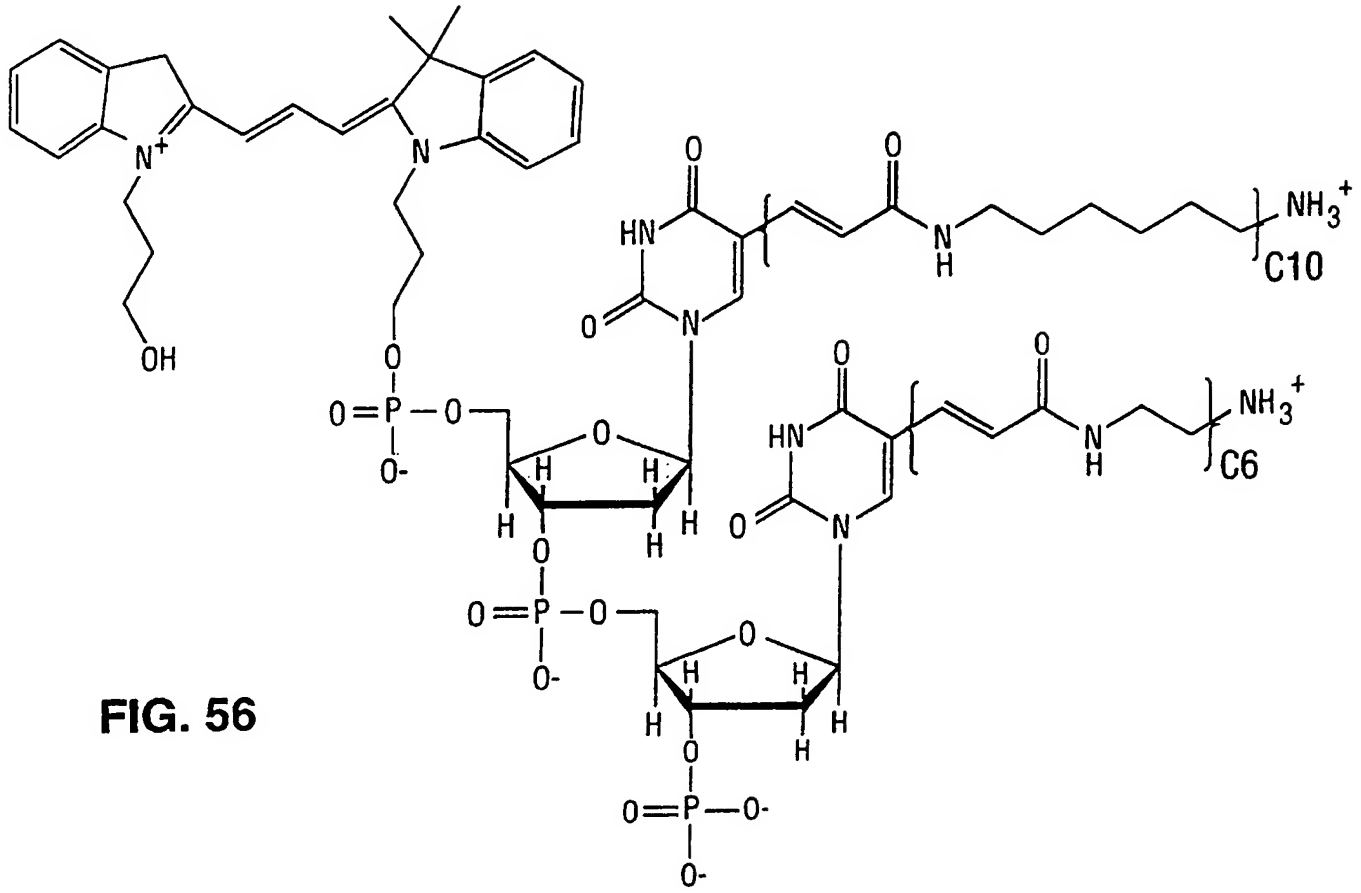


FIG. 55

70 (C10 amino T's)
74 (C6 amino T's)



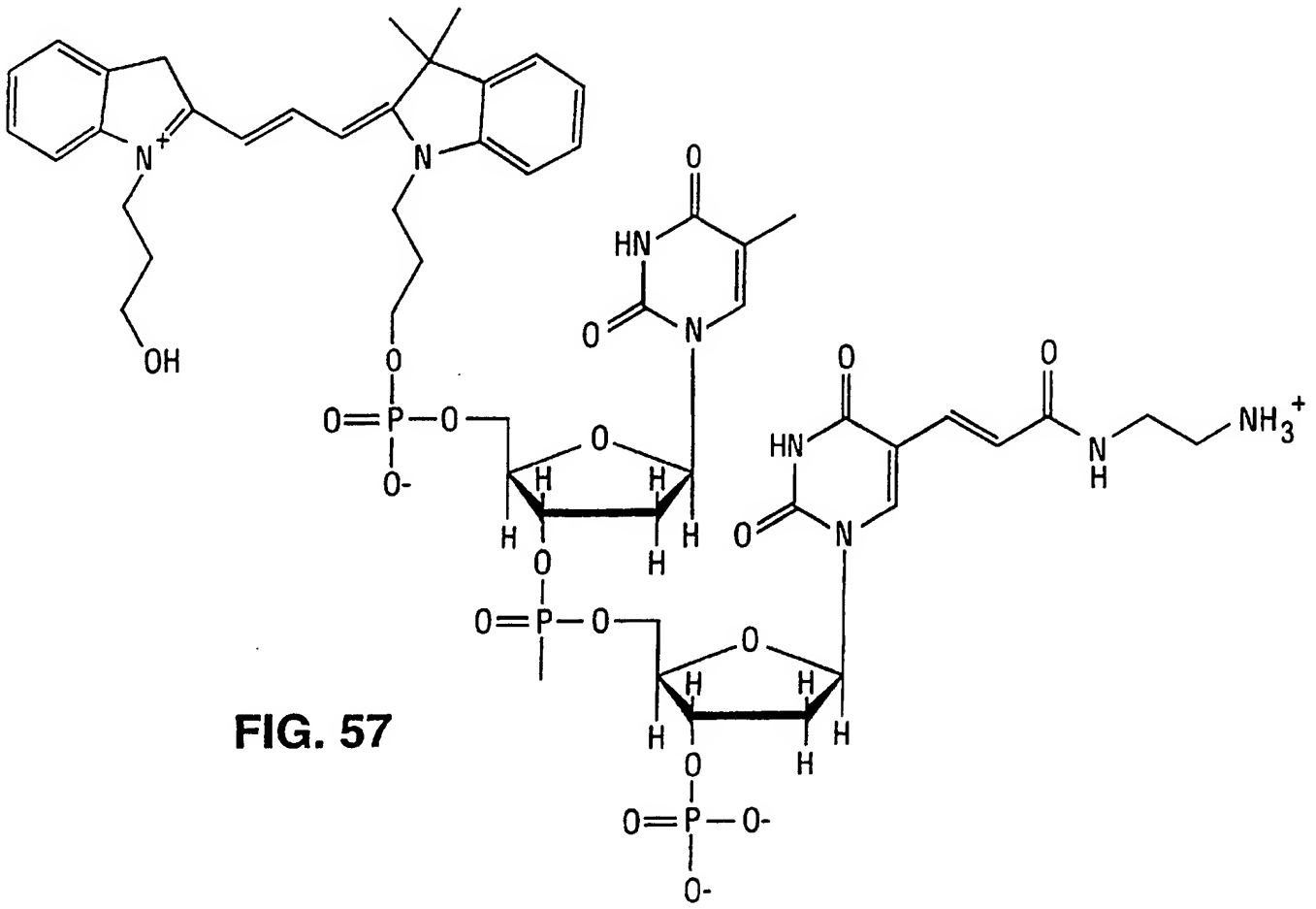


FIG. 57

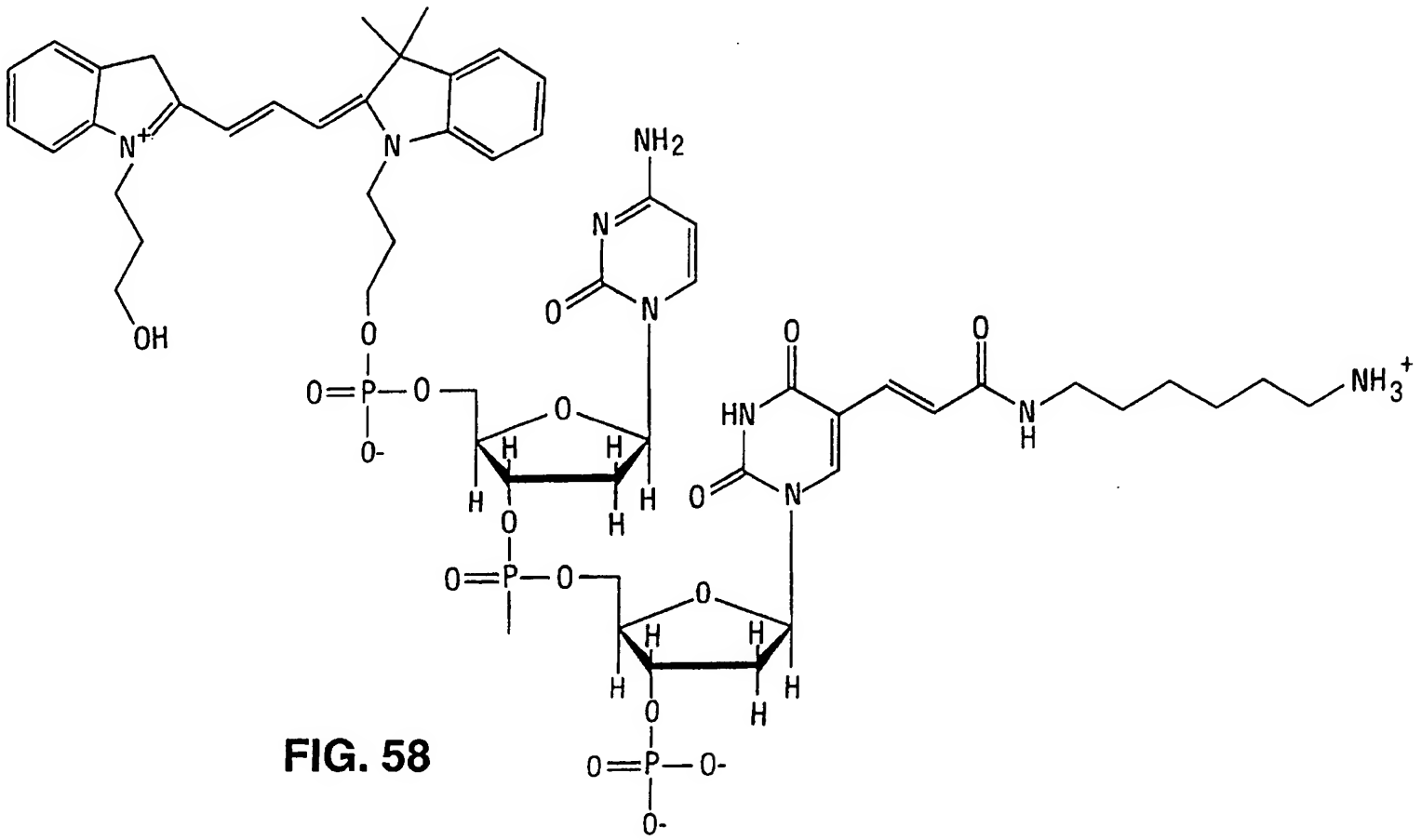


FIG. 58

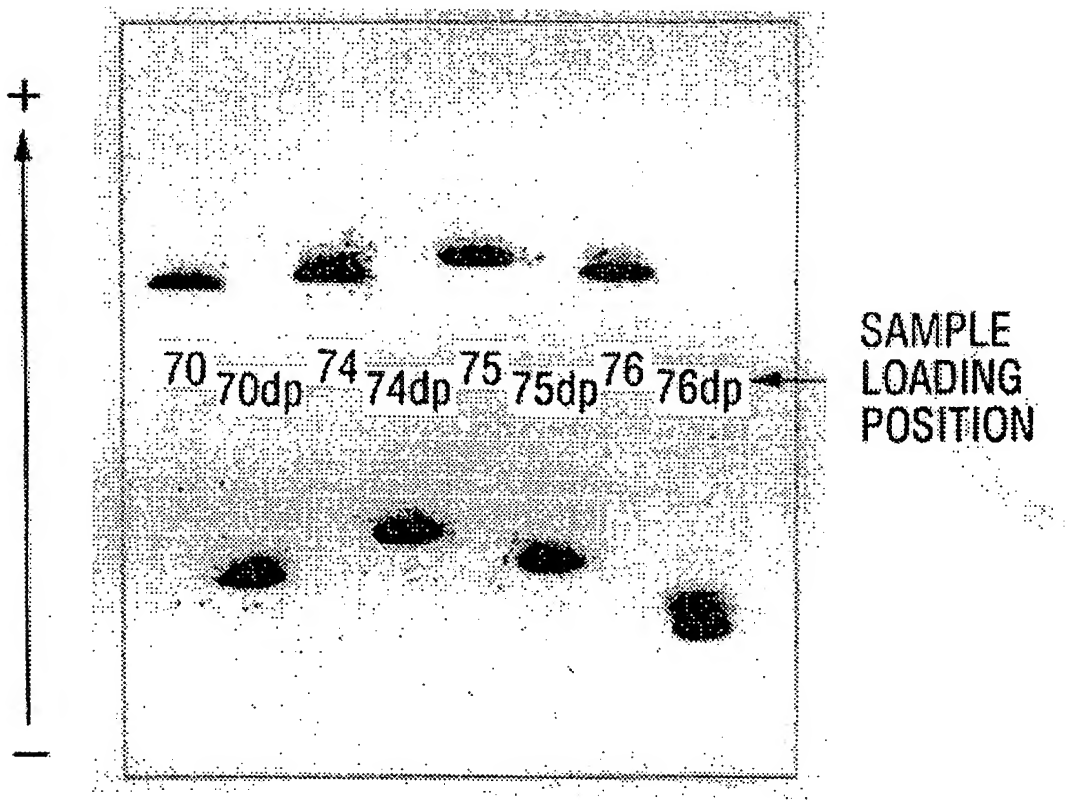


FIG. 59

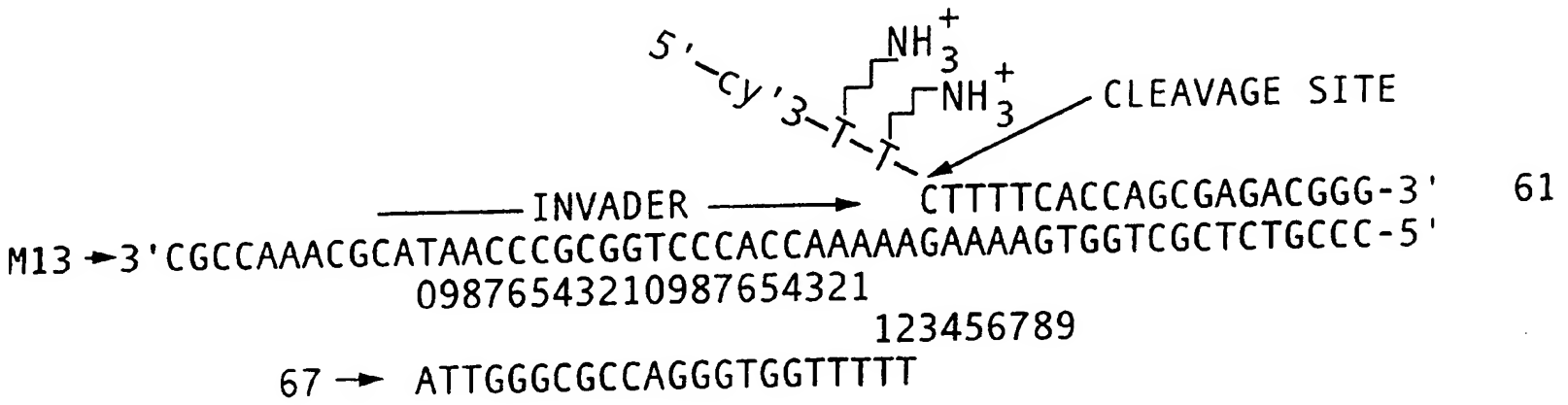

5'-Cy'3-T-T-
NH3+
NH3+
CLEAVAGE SITE
INVADER
CTTTTCACCAGCGAGACGGG-3'
61
M13 3'CGCCAAACGCATAACCCGCGGTCCCACCAAAAAGAAAAGTGGTCGCTCTGCCC-5'
09876543210987654321
123456789
67 ATTGGGCGCCAGGGTGGTTTTT

FIG. 60A

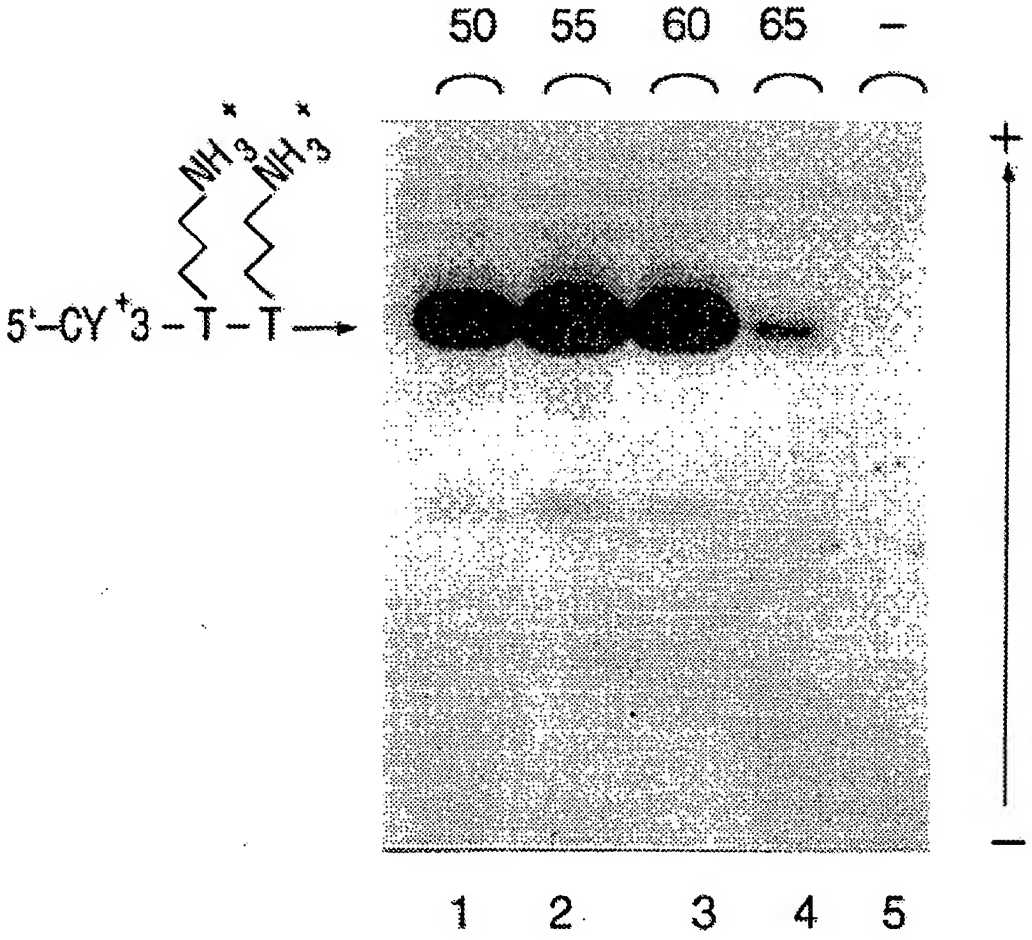


FIG. 60B

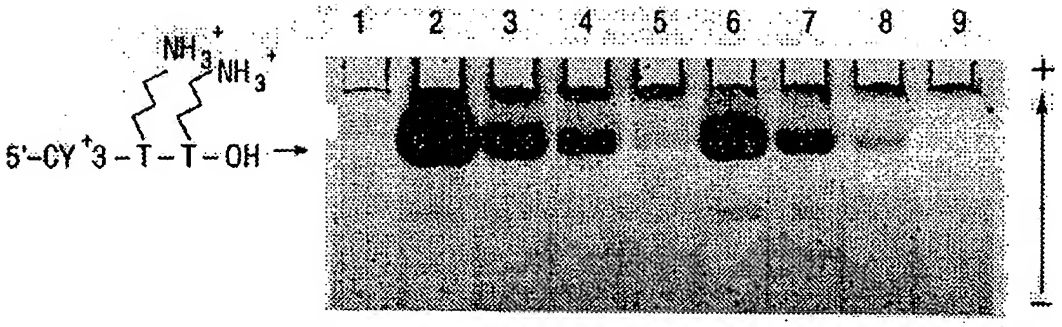


FIG. 61

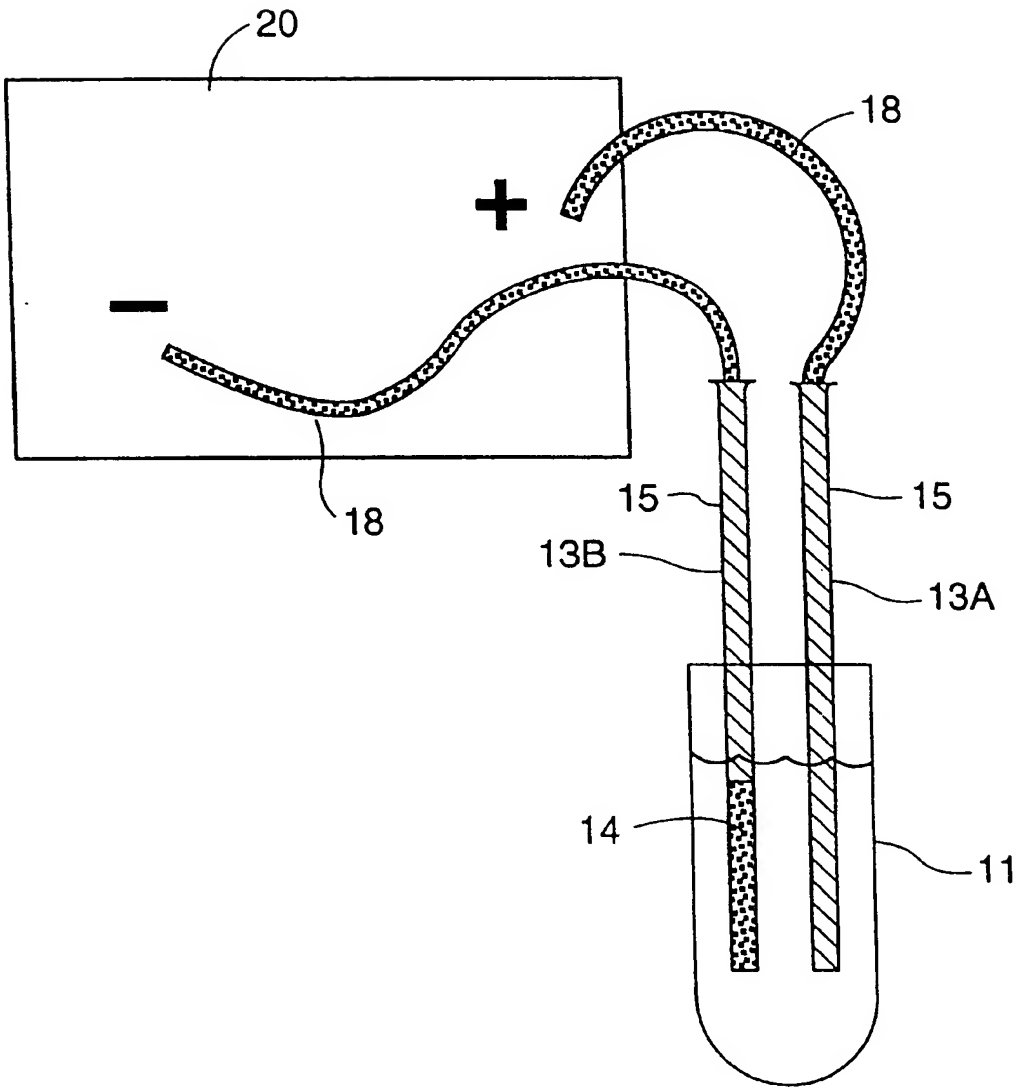


FIG. 62

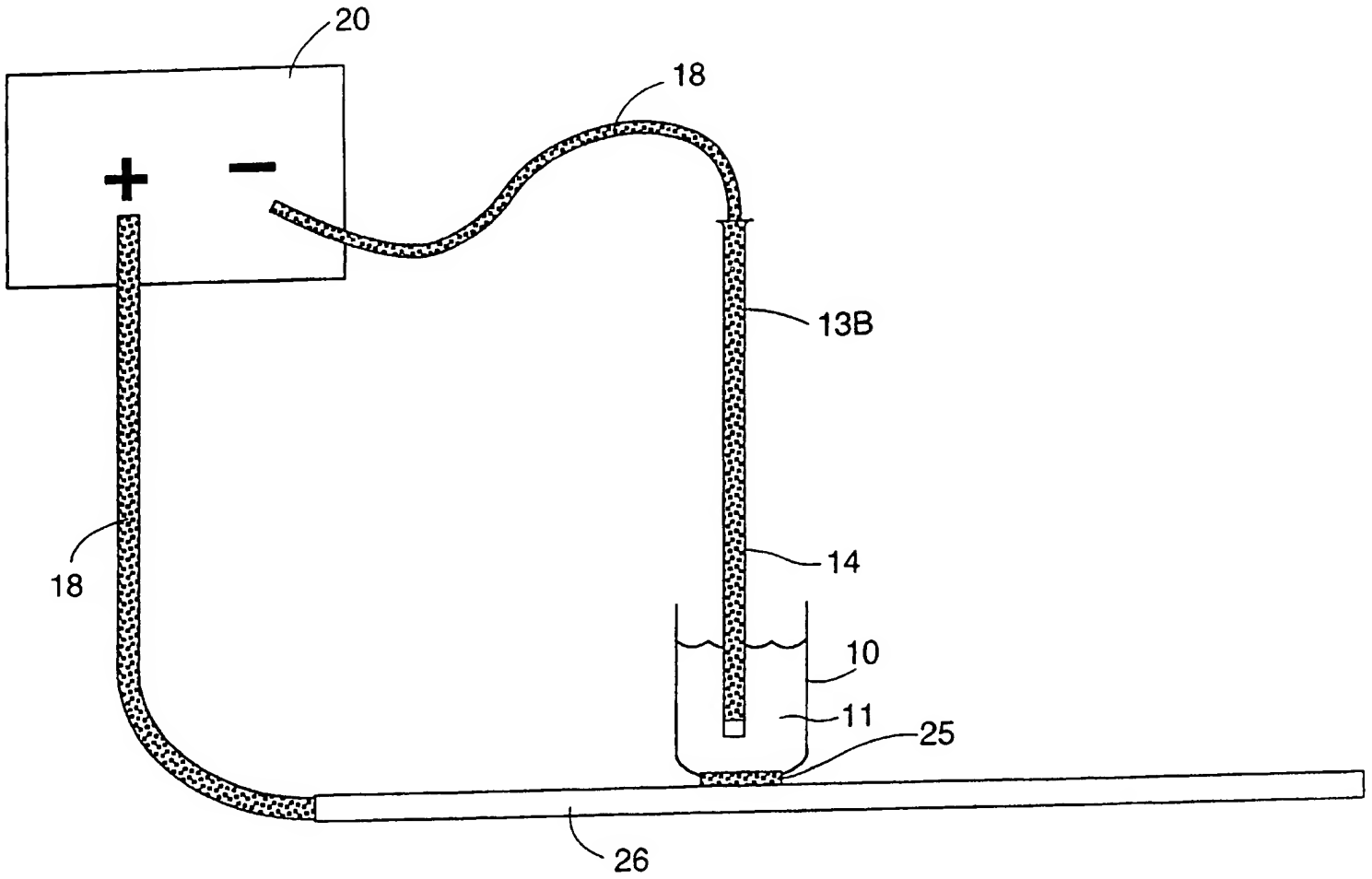


FIG. 63

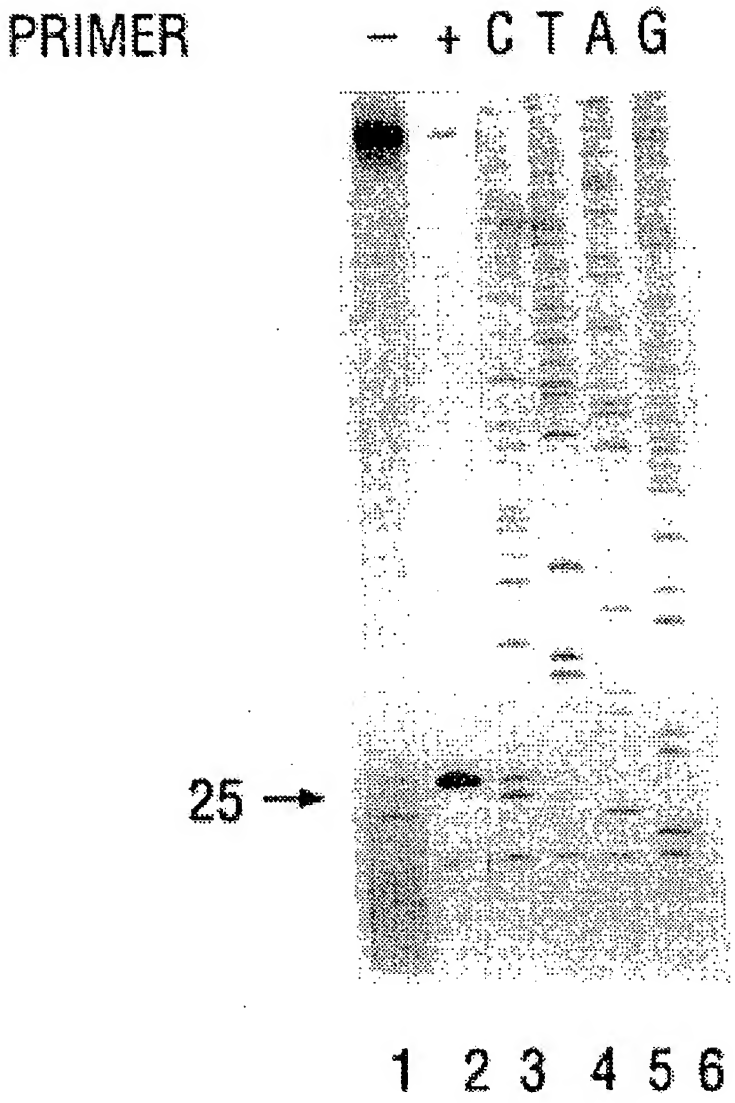


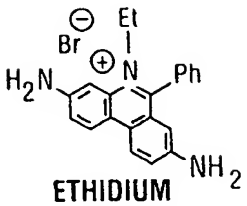
FIG. 64

FIG. 65A

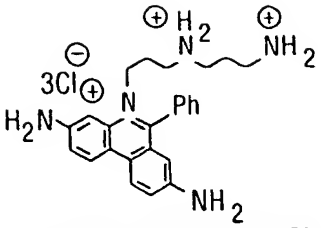
FIG. 65B

FIG. 65C

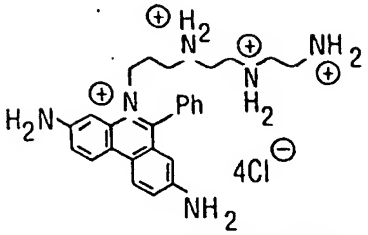
FIG. 65D



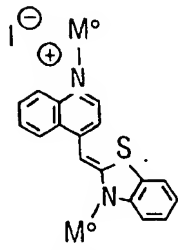
ETHIDIUM BROMIDE



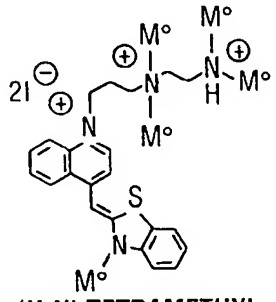
(1,3-PROPANEDIAMINO)-PROPIDIUM



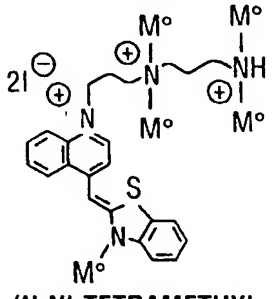
(DIETHYLENETRIAMINO)-PROPIDIUM



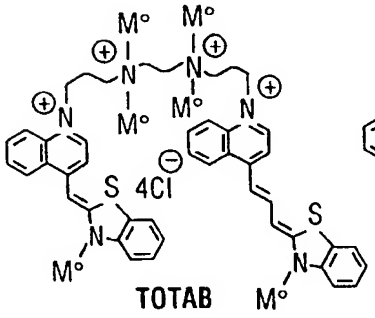
THIAZOLE ORANGE



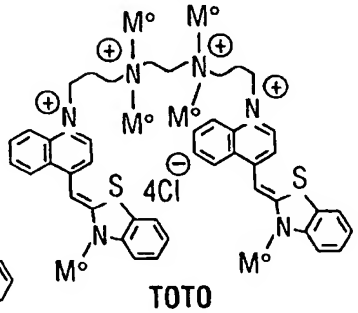
(N-N'-TETRAMETHYL-1,2-ETHANEDIAMINO)-PROPYL THIAZOLE ORANGE



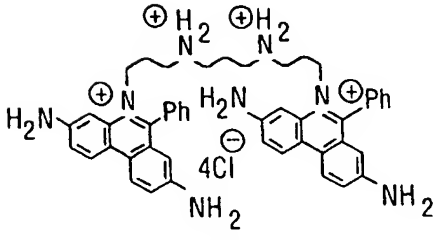
(N-N'-TETRAMETHYL-1,3-PROPANEDIAMINO)-PROPYL THIAZOLE ORANGE



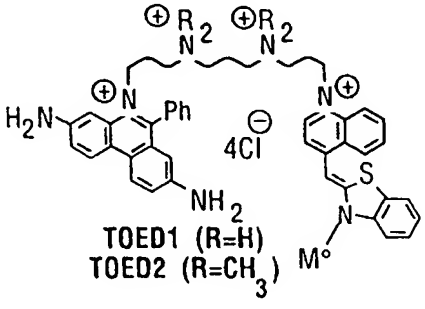
TOTAB



TOTO



EthD



TOED1 (R=H)
TOED2 (R=CH_3)

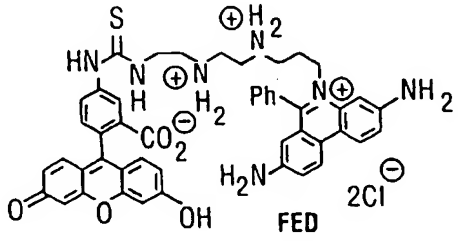


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FIG. 66